MODERN ASPECTS

OF THE

CIRCULATION IN HEALTH AND DISEASE

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SECOND EDITION, THOROUGHLY REVISED

ILLUSTRATED WITH 204 ENGRAVINGS

LEA & FEBIGER
PHILADELPHIA AND NEW YORK
1923

TO

OTTO FRANK,

IN APPRECIATIVE RECOGNITION

OF HIS MASTERFUL WORK,

THIS VOLUME IS

DEDICATED.

PREFACE.

No one who pauses to reflect can fail to admire the master minds of medicine, who, by simple signs and statistics, not only interpreted many disease processes correctly, but upon them built an admirable system of diagnosis. Nothing can be substituted for the power of accurate observation, either at the bedside or in the laboratory. Nevertheless, it happens that many phenomena of the circulation, normal and abnormal, remain undetected by our unaided senses. Consequently, various instrumental methods have been introduced which supplement our direct observations either by recording the functions of the circulation graphically or by translating them into numerical terms which the mind can more definitely grasp.

This monograph deals with the ways in which the application of laboratory methods to the clinic has led to the elucidation of many obscure conditions, to the recognition of new diseases and to the institution of new forms of treatment. In order to present the subject in the consecutive and logical manner necessary for academic purposes, and still retain the convenient arrangement demanded of a reference medium, it has been divided into three sections.

The chapters of the first section attempt to present our most modern conceptions as to how the circulation is maintained in health. This is of fundamental importance, for no one can essay to discuss the abnormal conditions of the circulation from a modern standpoint without constant reference to the fundamental physiological conceptions. Unfortunately, in some respects, many of our current views must be revised to accord with the facts brought to light by the application of more improved methods in experimental investigation. Hence, it is desirable not only to review our new acquisitions of knowledge and fit these in with those long accepted, but to describe, to some extent, the principles of the newer apparatus by which they are obtained.

The second section deals with the various instruments and procedures which are available for studying the circulation of man. Its purpose is more far-reaching than to serve as a mere catalogue of apparatus or a chronicle of "procedures" and "interpretations." It attempts, above all, to place a correct valuation upon different forms of apparatus and to point out their limitations and errors. To do this justly would be an impossible task were the question, as in the

past, still a matter for individual opinion or preference. Fortunately, however, matters have recently changed. Through the painstaking analyses of men like Frank, Einthoven and their associates, the enormous value of whose contributions is still imperfectly appreciated, the principles underlying the construction and evaluation of an instrument have been carefully evolved. Consequently, it is now possible, not only to construct mechanical apparatus along scientific lines, but also to ascertain definitely the defects and the limitations of that already in existence.

In the chapters comprising the third section the effort has been made to correlate the data obtained by experimental investigation of abnormal conditions in the laboratory with the results derived from the application of instrumental methods at the bedside and then to relate these, in turn, with the simpler signs and symptoms of the clinic. Careful study has shown that such a comparison of different procedures nowise diminishes the value of simple diagnostic criteria, but, on the contrary, often gives them an added significance or a clearer meaning.

During the eight years that have elapsed since the first edition of this monograph appeared, not only have many noteworthy contributions been made to our understanding of the circulation in health and disease, but many of our earlier conceptions again need revision and new phases demand greater consideration.

In order to meet the requirements of laboratory and clinical investigations as well as students and practitioners of medicine, the revision of a monograph upon the circulation may not content itself with the mere addition of the current advances; it must separate the chaff from the wheat, fit in that which is revolutionary in the new with that which is safe and conservative in the old, and above all relate the whole as a connected and practical narrative.

While the general plan of the original edition has been retained, it was found necessary not only to recast and extend a large number of the chapters, but to add new chapters dealing with: The Efficiency and Adaptability of the Heart, The Vascular Control of the Circulation, The Principles and Practice of Optical Registration, The Functional Disturbances of the Heart and The Dynamic Consequences of Arrhythmias and Chronic Heart Disease. This increase in scope has unavoidably increased the size; but not in proportion to the increase in subject-matter. The illustrations, so necessary to a clear interpretation of the subject-matter have practically been doubled in number, in spite of the fact that many of the older illustrations have been deleted. It is probable that in the reading or digestion of so great a literature as has grown about the subject, some errors of omission and commission have been made. For their correction, the author invites the coöperation of the reader. Attention may be called to the fact, however, that the original conclusions

are not always accredited to the investigator in question when it has appeared to the author that they were unwarranted by the data or when they seem to read counter to facts. In general, it has been the endeavor to present the facts and data in preference to the "conclusions." The literature has been carefully revised to include the more important recent contributions.

Throughout the book, the author has incorporated the results of his own investigations on the circulation extending now over a period of nineteen years. Some of his more recent work appears here for the first time. Similarly, it has been possible, with their kind permission, to introduce several unpublished reports of the recent work of a number of colleagues.

I am indebted to my many friends for illustrations accredited to them throughout the book, to my secretary, Miss Sara F. Donnelly, for her painstaking efforts in preparing the manuscript and verifying references, and finally to the publishers, Messrs. Lea & Febiger, for their splendid spirit of coöperation.

C. J. W.

Cleveland, 1923.

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SECTION I.

PHYSIOLOGY OF THE CIRCULATION.

CHAPTER I.

THE PHYSIOLOGICAL PROPERTIES OF THE HEART AND THEIR CONTROL.

Our information regarding the nature of the heart beat has largely been built upon the conception that cardiac tissue is endowed with four fundamental properties: *Rhythmicity*, the power of originating its impulse; *conductivity*, the power of transmitting the impulse; *irritability*, the power of responding to an impulse or irritant, and *contractility*, the power of changing its shape and length in response to excitation. To these may probably be added a fifth function, *tonicity*, or the power of sustained partial contraction by virtue of which it resists stretching.

While these properties are generally acknowledged as descriptive of definite phenomena connected with the heart beat, there is still some divergence of opinion as to whether they represent independent processes mediated by specific energy transformations within the cells and capable of varying in diverse directions (Englemann); or, whether they are interdependent processes, fundamentally due to the same energy transformation and, therefore, capable of varying only in the same direction. Recent evidence tends to strengthen the latter belief (Frey, Lewis and Drury, Tait).

METHODS OF STUDYING THE HEART BEAT.

The Myographic Study of the Heart Beat.—The registration of the mechanical contraction and relaxation of the heart has been of great value. By recording the rapidity and amplitude of contraction, the

phenomena of contractility and irritability have been studied; the latter, on the assumption that if the impulse may be regarded as of constant intensity, then the amplitude is an index of irritability. By recording the rate and extent of active relaxation the tonicity has been investigated. By estimating the time difference between the beginning of contractions recorded from several different regions the rate of conductivity has been studied. Thus, the difference between the beginning of auricular and ventricular contractions (the so-called *As–Vs* interval) has frequently been used as a measure of the conduction time. By recording and, still better, by careful observation of the sequence and priority of contraction in separate portions of the heart, the region in which rhythmicity predominates has been mapped out. It is apparent, therefore, that the accurate registration of the contractions from different regions of the heart is of great importance.

The simplest procedure by which this may be accomplished consists in fastening one end of a thread to any point of the heart and attaching the other to a simple lever of such efficiency that it follows, with a reasonable degree of accuracy, the movements of that point of the heart to which it is attached. Unfortunately, sufficient attention has not been paid to the efficiency of levers. This is evident from an inspection of the levers in use in many laboratories, as well as from a study of published records.

The factors that determine the efficiency of a lever are indicated by the formula $G = \frac{3}{v\,L\,\mu}$, in which G, the efficiency, is inversely proportionate to v, the magnification, L, the length of the lever, and μ, its unit mass (Frank). In other words, the best lever is theoretically the one with the lowest magnification, the shortest length and the lightest material. These qualifications have a practical limit. On account of a certain required rigidity, an infinitely light lever is also impracticable unless beams of light which record photographically are employed.

In the selection of ponderable levers one should choose, whenever possible, short, hollow straws tipped with light yet flexible pointers, and the magnification should be reduced to the lowest figure. It may be pointed out in this connection that physiologists have usually been too greatly concerned with obtaining records of large amplitude, and have been unaware that such have been secured at the expense of accuracy. Provided that friction between drum and pointer is minimized or, better, entirely avoided by photographic registration, records 10 to 15 mm. in amplitude are adequate for most purposes. In case larger records are needed, it would be far better to secure them by subsequent photographic enlargement, which can be done without a sacrifice of accuracy.

Instead of transmitting the movements of a point on the heart directly to a lever, it has been found more convenient to transfer them to a receiving capsule closed with rubber dam and then com-

municate the change by air transmission to a recording capsule of the Marey type. Although exceedingly convenient, such devices are always less efficient for the same amplitude of record than direct lever registrations. Their extensive use has, therefore, not added to the accuracy of the study of heart functions.

In determining the adequacy of the apparatus for the purpose in hand—*i. e.*, in satisfying oneself that the lever, on account of resonance effects and interference waves, does not distort the contour and height of curves and that the rise starts promptly—the physical principle, that the inherent vibration frequency of the apparatus must definitely exceed the highest rate of vibrations it attempts to record is applied. Thus, it is clearly impossible to make a second pendulum vibrate fifteen to thirty times per second. Feats no less ridiculous from a physical standpoint have, however, been attempted by physiologists. Thus, a lever with one or two inherent vibrations per second would be adequate to record the slow beats of a frog's or a tortoise's heart, but entirely inadequate to record the contractions of a rabbit's or cat's heart beating at a rate of 200 to 250 per minute.[1]

Given a lever or tambour system of such efficiency that the punctate movements of the heart are accurately recorded, the question still remains whether the movement of the point on the heart is an index of the amplitude of contraction. Obviously, this depends entirely on conditions. If the opposite point is fixed or stationary the movements of the chosen point will correspond well with variations in the length of the muscle fibers. This is the case of the perfused heart, in which the base is fixed by a cannula in the aorta and the movements of a point on the apex of the left ventricle are recorded. On the other hand, if the opposite point moves or the heart, as a whole, is dislocated then the variations of any point communicated to the most ideal lever give no reliable information as to the variations in the length of cardiac fibers.

To obviate this disadvantage in punctate registration various forms of *myocardiographs* (Cushny, Roy, Gesell, Wiggers) have been introduced. These instruments consist of two arms fastened by hooks or by stitches to the heart. One arm is stationary and the other movable. The movements of the latter are communicated either directly to a lever (Roy, Cushny) or through a transmission system to a recording tambour (Wiggers). The latter has the advantage that the oscillations can be led any distance by rubber tubing. The cardiograph (Fig. 1) attached to a Lombard pattern of a recording tambour can be fitted up so that it has a vibration frequency of 16 per second, while it remains sensitive enough to record the beat of the cat's heart. In this apparatus the lever moves up in systole, while in Cushny's myocardio-

[1] For a full consideration of the qualities of levers and the methods of registering the heart beat, consult Frank in Tigerstedt's Handbuch der physiologischen Methodik, 1911, **1**, part iv, 17, and 1913, **2**, part iv, 175.

graph the lever is raised during relaxation by a light spring and drawn down by the shortening of the heart. Since the entire instrument swings freely in all directions as the heart shifts its position, the actual shortening between two points is obtained independent of all secondary movements of the heart. To attain this end most efficiently, however, it is desirable to so attach the points that the distance between their attachments is not influenced passively by volume changes within the heart. It is more desirable, for instance, to attach the two arms to the anterior surface of the ventricles than to the lat-

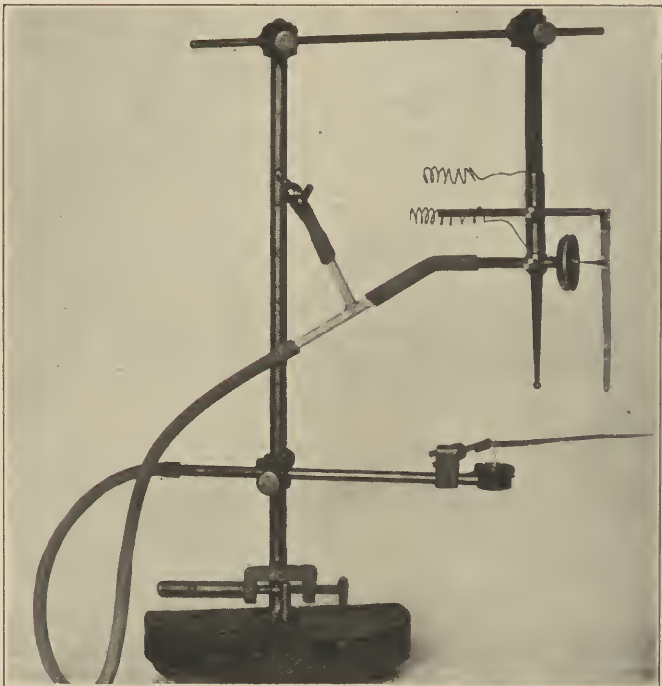

Fig. 1.—Cardiograph and recording tambour.

eral aspects; in which case the varying volumes of the left and right ventricles might modify the excursions. The construction of these instruments has so far necessitated the introduction of such considerable mass that it is questionable whether the recorded graphs are not distorted either by lever lag or fling or by a reaction of the entire mass of the instrument upon the heart.

As this is of great importance in accurately recording the contractions of the auricle, more delicate apparatus is required. The author has devised a miniature myocardiograph of high frequency and small mass, by means of which the approximation of any two points on the

auricular surface from 3 to 25 mm. apart may be studied. This instrument, shown in natural size in Fig. 2, weighs less than 2 gm. and is free from joints, pivots, axes or other mechanisms producing irregular friction. In order to study the sequence of contraction at different points on the auricular surface, a polymyograph has been used (Lewis, Feil and Stroud). Six lightly weighted hairs are attached by a small bead to the auricle and stretched by tiny weights over two bars. As the threads move from right to left during auricular contraction, their

Fig. 2.—Miniature myocardiograph for studying auricular contractions in mammals (actual size.)

shadow may be projected into the horizontal slit of a photokymograph and the relative movements of the points thus recorded photographically.

Records obtained by such refined means do not exclusively represent contraction and relaxation processes in auricular tissue. The auricles lying upon the movable bases of the ventricles tend to move downward and rotate with each ventricular systole, while the rapid inflow of blood from auricle to ventricle during diastole tends to affect

passively the length of auricular tissue. As has been repeatedly emphasized by the author, such records must be interpreted with the greatest care.

The Electrographic Study of the Heart Beat.—The fact has long been known in physiology that whenever a tissue is excited the active portion becomes electrically negative to the resting portion. Hence, if an external conductor connects these portions an electric current flows, the electromotive force of which is determined, as in a battery, by the degree of activity, but the amperage of which is measured, according to Ohm's law, by the external resistance as well. This is called the *current of action.* If the tissue is so connected that first the portion under one electrode and later that under another is active, we obtain a current that flows first in one direction and then in the other, that is, *a diphasic current.*

Since the spread of the impulse is accompanied by a similar state of electrical negativity, it has been sought by this means to determine the origin and propagation of the cardiac impulse more definitely than is possible by mechanical registration.

Although action currents from the heart were studied as early as 1879 (Burdon-Sanderson, Waller, Bayliss and Starling) by means of the capillary electrometer, it was not until the string galvanometer was adapted to physiological purposes by Einthoven that this method was applied intensively to a study of the initiation and propagation of the impulse. A discussion of the principles, details and critique of this apparatus will be deferred to a later chapter (page 251). It is necessary, however, at once to consider the principles employed in obtaining electrical records from the heart.

For experimentally investigating the rhythmicity and conductivity of hearts, the poles of the string galvanometer are connected to suitable forms of nonpolarizable electrodes which may be placed directly upon the heart, but are more often connected by moist threads either stitched to the heart or cemented to its surface by a drop of coagulating blood.

Such *electrograms* (as electrical records taken directly from the heart are termed) have been utilized to determine: (*a*) The direction and path of the excitation wave; (*b*) its origin; and (*c*) its rate of propagation. The different procedures employed for these purposes are as follows:

(*a*) **Electrograms Taken from Base-apex Leads.**—When the base of the entire heart is connected to one electrode and the apex to another, a curve is recorded that contains three distinct waves, *P*, *R* and *T*, the latter being frequently a downward wave. The interval between the rise of the *P* and *R* waves is usually considered equal to the time required for the impulse to pass from its point of origin to the ventricular musculature. Any variation of this interval is, therefore, an indication of an altered conduction time from auricle to ventricle.

(*b*) **Electrograms from Unipolar Leads** (Fig. 3) (Wybauw, Eyster and Meek).—If an indifferent electrode is placed on some remote part of the body and the other is connected to different points of the heart, a deflection of the galvanometer string to which they are connected occurs as soon as a state of negativity develops beneath the cardiac electrode. If these deflections are recorded in connection with some adequate mechanical event, such as auricular or ventricular systole, heart sounds, etc., or with a simultaneous electrocardiogram taken from the limbs, it is possible to shift the heart electrode from point to point and determine the relative appearance of negativity on different portions of the cardiac surface; or, better still, if two galvanometers are available the incidence of negativity at two points may be established for the same cycles.

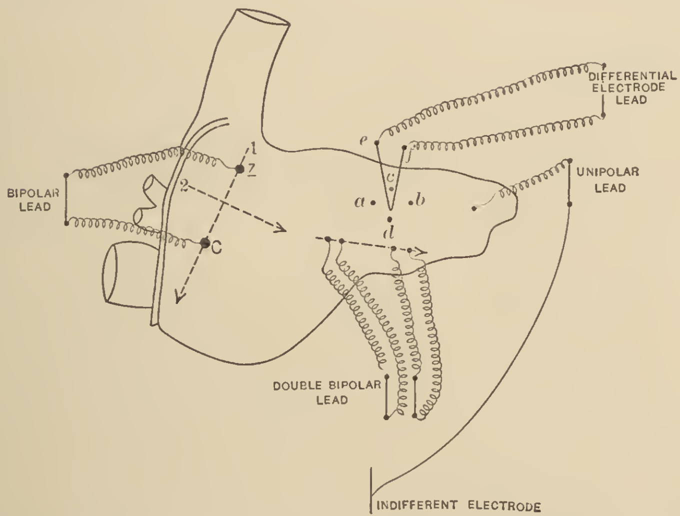

Fig. 3.—Diagram showing principles of different leading-off methods from auricular surface.

By charting the time of negativity at different points, it is possible to locate the point of earliest activity, or the *initial negativity*, as it is termed. This is the place of origin of the impulse. Further, by studying the points as regards the sequence of negativity, the spread of the excitation wave can be followed. Finally, the rate of propagation from point to point may be estimated. Thus, suppose one point on the auricular surface is negative 0.025 second after some studied cardiac event, while another part 12 mm. distant becomes negative 0.04 second after the same event, then it obviously required 0.015 second for the excitation to be propagated 12 mm., *i. e.*, the velocity equals 800 mm. per second.

It should be pointed out, however, that this cannot be taken to represent the conduction rate of the impulse unless it can be clearly shown that the impulse traveled in straight lines between these points.

(*c*) **Electrograms from Bipolar Leads** (Gotch, Lewis and associates, Eyster and Meek).—If two electrodes (*Z* and *C*, Fig. 3) are applied to a muscle sheet, some distance apart, negativity will develop first under the contact nearest to the source of excitation (*Z*) and later under the distal contact (*C*). The direction of movement of the string shadow can be so arranged that it records an upward deflection when negativity develops beneath *Z* and a downward deflection when negativity reaches *C*. If, at any time, the direction of the excitation wave is reversed under these contacts, so that it develops negativity at *C* before *Z*, the electrogram is reversed, showing first a negative and later a positive deflection. In this way the general direction of the impulse spread may be determined. In order to make out the exact lines of spread it is necessary to shift the two contacts through an angle of 90 degrees and determine the amplitude of deflection at each shift. Since the amplitude of the diphasic variations is greatest when the path of the impulse is in line with the electrodes, the exact line of spread is determined when the largest deflections obtain. Thus, in the case of the bipolar leads illustrated in Fig. 3, the largest deflection occurs when the excitation process follows arrow 1, while all other directions would cause a smaller deflection, that of arrow 2 showing no variations at all. Further, if these lines of spread be determined in a number of directions they must converge toward its origin. In this way the point of impulse initiation may be localized (*cf.* Lewis, Lectures on the Heart, page 8). In interpreting electrograms thus obtained, the difficulty must be recognized that the electrode contacts may receive not only currents from the excited muscle directly beneath, but occasionally also electrical changes derived from outlying muscle. The effect of this may be that a certain electrode may show evidence of initial positive potential when quite obviously initial negative potential is expected. By proper precautions these accidental *extrinsic deflections* may, however, be differentiated from *intrinsic deflections* which alone give true evidence of what is functionally taking place beneath the electrode (*cf.* Lewis, Meakins and White, l. c., page 384).

The bipolar method has also been employed to determine the velocity of conduction. If a positive deflection indicates negativity under electrode *Z* and the reversal to a negative deflection indicates negativity under *C*, then an estimate of the time required to travel the distance between the contacts is given. Certain sources of error may occur in this method of estimating conduction time. If negativity continues to predominate at *Z* after it has reached *C*, or, if by virtue of neighboring activity a predominance of negativity occurs at *C* in advance of the impulse, then the method does not give an accurate index of con-

duction time (Eyster and Meek). It is, therefore, important to rely only on such records as give sharp upward and downward deflections.

(*d*) **Electrograms from Double Sets of Bipolar Electrodes** (Lewis and associates, Eyster and Meek).—In determining the velocity of transmission between two points, as well as in determining the line of impulse transmission, the use of two sets of adjacent electrodes are always useful and often necessary (Fig. 3). The difference in the time of onset of the two curves is probably the most accurate measure of the interval of travel between the two regions to which electrodes are applied. By rotating the two electrodes of each set so that largest deflections are obtained, the line of spread may be accurately determined.

(*e*) **Electrograms from Differential Electrodes.**—In order to avoid the possibilities of error incident to the use of bipolar electrodes placed some distance apart in determining the direction of the impulse, but above all to make certain that changes in negativity beneath an electrode are due to activity of muscular tissue immediately under it, *i. e.*, that it is not transmitted to the surface from underlying active tissue, the so-called differential electrodes may be employed singly or in pairs (Clement, Erfmann). In this arrangement the two nonpolarizable electrodes of each set are connected by a sharply kinked, moist thread which makes a contact with the surface of the heart at the sharp bend, being attached either by an independent loop of thread or adherent by a drop of coagulating blood. In this way we really record the variation in negativity of two muscle points so close together that both lie under the string contact (Fig. 3). In such an arrangement the difference in potential is recorded only when the direction of the excitation wave is in the plane of the loop and fails to be recorded when the impulse travels at right angles or from the inside to the exterior of a cardiac chamber. Thus, in the scheme of differential electrodes shown in Fig. 3, an excitation wave passing from *a* to *b* causes the greatest possible difference in *ef*, while no deflection whatsoever follows when it passes from *c* to *d* or from the interior to the exterior. The criticism has been made, however, that the deflections recorded are either so small that they lead to error in measuring curves or that so great a loosening of the galvanometer string is necessary as to throw the accuracy of the records into question (Lewis, Eyster and Meek). As utilized in Garten's laboratory, these factors do not seem to have been serious, however.

(*f*) **Electrocardiograms from Body Surface Leads.**—When the electrical cardiac variations are led off indirectly from the surface of the body or the limbs, the records are designated as *electrocardiograms* (Einthoven). In this way currents conducted from one portion of the heart to another are tapped and from the records so obtained important evidence of the spread of conduction as well as velocity of conduction can be obtained without opening the thorax and exposing the heart.

While this method has been particularly developed as a clinical aid in the interpretation of conduction processes, and will, therefore, be considered in detail later (*cf.* page 268), it has also been of great service in experimental work on animals.

THE PHYSIOLOGICAL PROPERTIES OF THE HEART.

Rhythmicity.—Stannius, by his classical experiment, established almost conclusively that the beat of the cold-blooded heart starts peripheral to the auricle. While some difference of opinion still exists as to the precise seat of origin, the bulk of evidence indicates that it is near the sino-auricular junction rather than at the junction of the sinus venosus andente ring veins (Gaskell, Englemann, Meek and Eyster, Schlomovitz and Chase). Stannius's experiment consisted in tying a ligature about the sino-auricular junction, whereupon the beat of the auricle and ventricle ceased while that of the sinus venosus continued. Inasmuch as the human heart is evolved from an embryonic organ in which a sinus venosus region is present (His), it seems logical to assume that the remains of the sinus tissue probably constitutes the rhythmic area.

The question naturally follows, What becomes of the sinus region in the mammalian heart? Studies in comparative anatomy show that while the cavities of the sinus, auricle and ventricle are in direct communication, the musculature of the auricle is not interposed between sinus and ventricle, but rather superimposed upon the connecting band, known in comparative anatomy as the *canalis auricularis* (Mall). In the mammalian heart the sinus tissue has become submerged in the musculature forming the posterior portion of the auricle between the openings of the superior vena cava above and the coronary sinus below. Within this region lies a special knot of heart tissue, the sino-auricular or *S–A* node (Keith and Flack). This node, situated in the groove called the "sulcus terminalis," and bounded by a vascular circle from the right posterior circumflex branch of the coronary artery (Keith, Haas), is a club-shaped mass, its headlike enlargements sending a few strands up to the superior vena cava, its lower end terminating midway between the superior vena cava and the coronary sinus.

Embryological and developmental studies on the same species and comparative studies of different species indicate that a part of the original sinus tissue enters into the formation of this node, the remainder becoming condensed into the auricular part of the *A–V* node (Koch, Keith, Mackenzie, Külbs, Aschoff). Histologically, the *S–A* node is composed of delicate, fusiform, interlacing muscle fibers embedded in a densely packed connective tissue. The fibers are pale in color, faintly striated and contain elongated nuclei. The muscle fibers are small as compared with ordinary auricular muscle and the sarcoplasm contains relatively small amounts of glycogen.

The node is not entirely a muscular structure, however, as was originally supposed, but contains many nerve fibers and fibrils and a few ganglion cells (Oppenheimer and Oppenheimer).

The S–A Node as Pacemaker.—Keith and Flack suggested that the S–A node represents an important part of the original sinus tissue and Lewis has designated it the *pacemaker* of the heart. The experimental evidence in favor of this view is: (1) That excision or destruction of this node generally causes a *cessation* or slowing of the auricular beat (Hering, Cohn, Kessel and Mason, Moorhouse); (2) that changes in temperature ranging near to those of the body produce alterations in the rate of impulse initiations only when they are applied over the S–A node.[1] As may be expected, cooling decreases and heating increases the rate (Brandenburg and Hoffmann, Ganter and Zahn, Zahn, Schlomovitz and Chase); (3) that the node becomes electrically negative before the neighboring regions (Wybauw, Lewis, Lewis, Oppenheimer and Oppenheimer, Eyster and Meek, Garten and collaborators).

Ectopic Rhythmic Centers.—The S–A node is by no means the only locality in which the impulse actuating the heart beat can originate, but the seat of impulse formation may shift for a longer or shorter time to some other portion of the conducting system. Such centers are designated as *ectopic* (Lewis) or *heterotopic* (Hering). As a result of extensive histological investigations (His, Tawara, Braeunig, Retzer, De Witt and others), it has been shown that a very distinctive system of muscle fibers lies enclosed within its own sheath beneath the endocardium. This may be spoken of as the *His-Tawara system.* It begins as a few strands of muscle fibers in the region of the coronary sinus. These converge toward a thickening spoken of as the *auriculo-ventricular node* (Tawara), or, more correctly, perhaps the *sino-ventricular node.* From this node a thin strand passes across the auriculo-ventricular septum, forming *the bundle first described by His and bearing his name.* It courses downward and forward, reaching the membranomuscular junction of the interventricular septum. Here it divides into two branches which pass subendocardially—one to the left and the other to the right ventricle. These, in turn, divide and redivide, some strands crossing the cavity of the ventricle as "false cords," others dividing more and more, forming eventually an extensive arborization on the inner surface of the ventricular walls (Fig. 4). Embryological studies have shown that the A–V node, lying at the posterior and right border of the interauricular septum, is divisible into two portions: (*a*) *An auricular part or coronary sinus portion,* derived in common with the S–A node from the primitive sinus tissue, and (*b*) *a ventricular portion,* derived from the tissue of the auricular canal (Koch, Aschoff). Histologically, the muscle cells composing

[1] For an analysis of experiments showing contrary effects after destruction of the node or as a result of application of temperature, the comprehensive review of Eyster and Meek should be consulted (Physiological Reviews, 1921, 1, 1).

this system differ in their general appearance in various regions. The cells of the auriculo-ventricular node resemble those of the sinus node, but, as the strand passes into the bundle of His, their character changes suddenly. As we follow the cells from this bundle to their final arborization, it is found that in general the cells become larger, have more sarcoplasm and striations, the nuclei become larger and more numerous, while the glycogen content increases (Nagayo, Rojas); in short, they assume the characteristics long ascribed by *Purkinje to the peculiar cardiac fibers that bear his name.*[1] Histological studies of

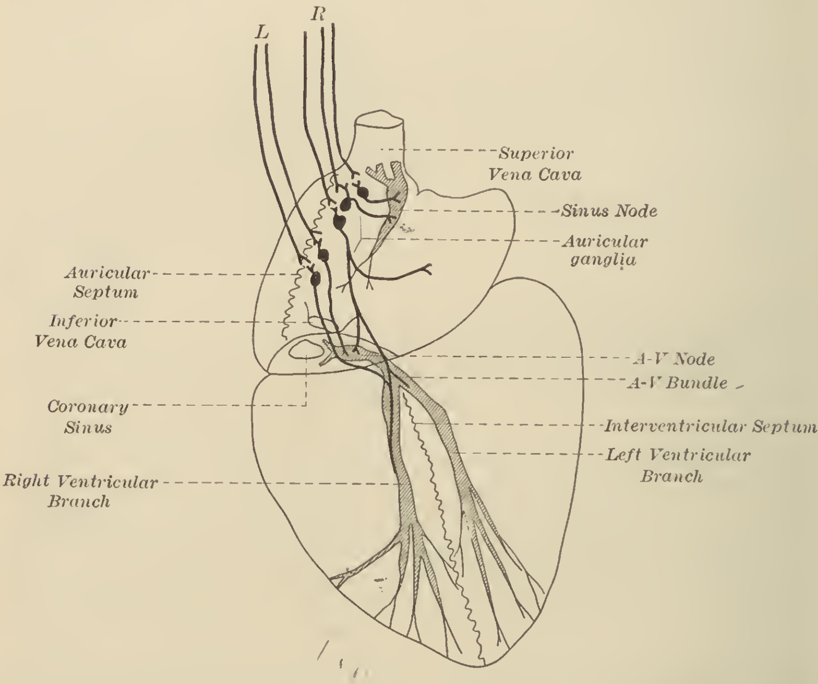

Fig. 4.—Schematic figure showing relations of sinus node, *A–V* node, *A–V* bundle, His-Tawara branches as well as probable connections of ganglion cells and extrinsic nerve fibers. *R*, right vagus; *L*, left vagus.

fresh material (Van der Stricht and Todd) (which alone is suitable for detailed histological study on account of the tendency to produce abnormalities by postmortem glycogenolysis) indicate that throughout the His-Tawara system several types of fibers are present, viz.:

(*a*) Embryonic types, containing multiple nuclei, clustered together or located axially in a clear sarcoplasm. In the periphery of these cells are found longitudinal striations running either in a parallel or intercoursing manner.

[1] For a detailed review of the muscle systems of the human heart, see Mönckeberg· Ergebnisse d. allg. Path. u. path. Anat., 1921, **19**, 328.

(*b*) Adult types, longer and larger than the former and containing multiple nuclei which are distributed more toward the periphery as well as toward the poles of the cells. The longitudinal striations are relatively more numerous and not limited to the periphery of the cells. Toward the ends they either have a tendency to separate into distinct strands, presaging a longitudinal cleavage actually found in other more advanced types.

(*c*) Transitional cells, which connect the Purkinje cells proper with ordinary ventricular muscle. The myofibrils increase, the sarcoplasm diminishes and other cells become smaller and more slender, finally merging either abruptly or gradually with ventricular muscle cells.

Like the *S–A* node, this His-Tawara system is also a neuro-muscular structure, for not only are separate nerve fibers distributed through it, but distinct bundles and trunks of nerves are present. In addition, ganglion cells are found (Wilson, Engel, De Witt).

Experimental work has shown that various portions of this His-Tawara system may become the seat of rhythms designated as ectopic. Thus, if the *S–A* node is either depressed or destroyed (*e. g.*, by crushing, removal, formalin, cold, clamping, inflammation), or if the irritability of the *A–V* node is raised, the latter assumes the role of initiating the heart beat (Zahn, Meek and Eyster). When the "pacemaker" is thus transferred to the *A–V* node, as a result of injury or destruction of the *S–A* node, the seat of impulse formation is usually transferred to the coronary portion of the *A–V* node, although occasionally it may shift to the ventricular portion. In the former case, the *As–Vs* intervals approach normal; in the latter, they are much abridged (Meek and Eyster). A shifting of the "pacemaker" to the *A–V* node may also be brought about by raising its irritability. Thus, when the *A–V* node is heated by a specially constructed thermode, the impulse initiation may take place either in the coronary or the ventricular portion of this node depending on the point that is warmed. Again, it has been found that if the impulse in such cases originates from the coronary portion no reduction in the *As–Vs* interval takes place, while the interval is appreciably abridged if the impulses arise from the ventricular portion (Zahn). Since many nervous mechanisms modify the relative irritability of these structures it is extremely probable that there is normally more or less shifting of the pacemaker not only within one node but from one node to the other. In consequence, it is necessary to bear in mind that certain cases of cardiac acceleration are due not to a hyperactivity of the *S–A* node, but to the fact that the "pacemaker" has shifted to the coronary portion of the *A–V* node.

If the ventricles for any reason are cut off both from the *S–A* and *A–V* node (*e. g.*, when the His bundle is cut, clamped or destroyed) they develop a rhythm of their own, termed the *idio-ventricular rhythm.* The rate and development of this rhythm is determined by the rate

at which the ventricle beats previous to its separation, the rhythmic center being less active if the ventricular rate was previously rapid (Erlanger, Cushny). Since we have evidence that under such conditions both ventricles receive their excitations over natural pathways (*cf.* page 497) and that they contract in a coördinated manner, it is probable that, in such instances, the rhythmic center is located in the His bundle just peripheral to the section, compression or damage.

Finally, it is possible that still other portions of the heart may become the center of impulse initiation. Thus, if both bundles are cut, a still lower center assumes the rhythm (Eppinger and Rothberger). As their order of rhythmicity is very low, it is doubtful whether these areas can ever dominate the rhythm of the heart. Their importance consists rather in the fact that they serve to disturb some other dominant rhythm, as in the case of premature systoles. In the case of the ventricles the probable seat of such ectopic beats may be the ventricular muscles themselves, less likely the terminal arborization of the His-Tawara system; in the auricles the posterior wall of the right auricle and interauricular septum appear to have a somewhat higher order of rhythmicity (Erlanger, Moorhouse).

From these facts a picture of the processes of impulse initiation has gradually been formed: It appears that a form of metabolic activity occurs in a large number of regions of the heart which enables each of these to accumulate energy to a certain level and then discharge spontaneously as a muscle impulse. The rate of metabolic activity stands in the following order: *S–A* node, *A–V* node, His bundle, separate bundles, etc. Consequently, the rate of discharge stands in the same order. If several such centers are simultaneously active the rate of the heart, as a whole, will be dominated by that center which discharges most frequently; for not only does it set the pace, but it causes in all other centers a discharge of impulses which are presumably ineffective or subminimal even when they do not happen to fall during a refractory phase of the cardiac muscle. When, however, a more rapidly discharging center, such as the *S–A* node, is in abeyance, then the *A–V* node rhythmically, but at a somewhat lower rate, sets the rhythm for the heart. When this node in turn is not functioning the *A–V* bundle develops rhythmicity at a still lower rate. Beyond this point, however, the order of rhythmicity diminishes rapidly and it has not yet been demonstrated, with any degree of certainty, that tissues aside from those mentioned are able to maintain consecutive rhythmic beats for the heart.[1]

Conduction.—By what paths and in what manner are the impulses propagated to the auricles and ventricles so that they beat in definite sequence?

[1] Greene and Gilbert (Am. Jour. Physiol., 1922, **60**, 170) report what seems to be the first instance of a rhythmic center in the left branch of the His-Tawara bundle.

Sino-auricular and Sino-ventricular Conduction.—All experimental work indicates that no differentiated paths of conduction exist in the auricle, but that impulses spread radially from different borders of the *S–A* node over ordinary auricular tissue at velocities ranging from 600 to 1200 mm. per second (Lewis, Meakins and White). The spread occurs over muscle bundles which appear to originate in close proximity to the *S–A* node and radiate in fan-shaped manner to various portions of the right and left auricle (Keith, Papez). To the left, auricle impulses probably pass with greatest facility by the interauricular band (Bachmann, Papez). The rate of spread through the muscle band is such that the excitation wave, as gauged by the appearance of electrical negativity, reaches the right auricular tissue in about 0.02 second, the right appendix in about 0.03 second and the left appendix in about 0.045 second (Fig. 151, A.)

The chief question still at issue is the manner in which impulses are conducted to the *A–V* node. Most histologists have concluded that no differentiated tissue exists between these two nodes, but that the endings of both nodes fade away into surrounding auricular tissue (Keith and Mackenzie, Koch, Aschoff and Mönckeberg, Pace). The possibility must be borne in mind, however, that the work of those investigators who have reported definite connections may still be confirmed (Curran, Thorel).

While all experimental work also indicates that conduction waves spread diffusely and not through limited paths between the *S–A* and *A–V* nodes, two views have gradually developed as to how the impulses travel preferentially to the *A–V* node. According to one view, the impulses reach the *A–V* node by way of atrial muscle, *i. e.*, is excited relatively late (Lewis, Meakins and White); according to another, the atrial tissue and *S–A* nodes receive their excitations over different routes (*cf.* Fig. 158) (Eyster and Meek). According to the latter view, a slight delay exists in the transmission of impulses from the *S–A* node to auricular tissue, while the impulses in many instances pass with somewhat greater rapidity over the tissue joining the *A–V* and *S–A* nodes. In consequence, the *A–V* tissue becomes negative about 0.023 to 0.03 second after the *S–A* node and distinctly in advance of that of the right auricle (Eyster and Meek). According to the former view, the velocity of conduction is equal over all routes and the *A–V* node becomes negative 0.03 to 0.04 second after the *S–A* node, and, therefore, never precedes the negativity of the right auricle (Lewis, Lewis, Meakins and White).

Conduction in the Ventricles.—There remains no doubt that the impulses are conducted to the ventricles by the His-Tawara system. The only question that can arise is whether the nerve fibers or the muscle elements within this system are responsible for this condition. Experimental evidence does not favor nervous conduction, however, for: (1) Histological examination has shown that many fibers termi-

nate in the muscle cells directly; (2) conductivity fails to occur after recovery from crushing, when muscle tissue does not degenerate but nerve fibers do so (Erlanger); and (3) application of cocaine, which paralyzes nerve fibers does not produce *A–V* block (Cullis and Dixon).

The velocity of conduction varies in different portions of the His-Tawara system; it is most rapid in the Purkinje tissue of the bundle and its branches (3000 to 5000 mm. per second), much slower in ventricular muscle itself (400 mm. per second) and slowest in the *A–V* node (probably 200 mm. per second). Lewis has drawn attention to the fact that the order of conductivity stands in direct relation to the glycogen content of these fibers (Nagayo), but this does not neces-

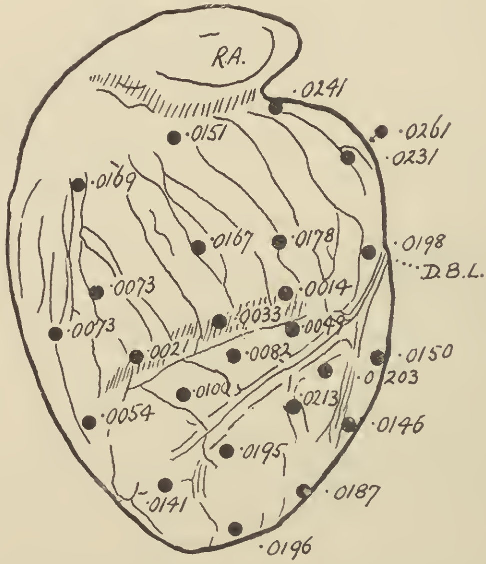

FIG. 5.—Outline of front of the heart showing relative time of excitation as related to R_2 of electrocardiogram. (After Lewis.)

sarily indicate any functional relationship, especially as the order of rhythmicity with which glycogen metabolism might possibly be concerned (*cf.* page 30) is inversely related to the glycogen content.

Impulses reaching the *A–V* node are delayed here for an interval of about 0.05 second. According to Zahn, it is possible to show that this delay actually occurs in the middle portion of the node. They then shoot through the His bundle and its branches at a high velocity, reaching their termination within another 0.01 to 0.015 second. Two things are accomplished by these variable conduction rates: The delay in the *A–V* node prevents the excitation of the ventricles previous to that of the auricular appendages, and the rapid rate of transmission through the bundles ensures the arrival of the impulse at the terminal

arborization at approximately the same time. From these terminal arborizations, impulses are transferred by the transitional cells of the Purkinje system to ordinary ventricular fibers on the internal aspect of the ventricles. Thence, they are conducted toward the surface by ordinary ventricular muscle. As the rate of conduction to these fibers is much slower and the impulse must traverse layers of varying thickness, it follows that not all muscular elements of the ventricles can be excited absolutely at the same time. The experimental work of Erfmann, who found that various portions of the ventral aspects of the ventricles become negative within a few thousandths of a second of each other, indicates that the differences are negligible and that for dynamic purposes the ventricular fibers may be regarded as excited simultaneously. Lewis and Rothschild, however, found differences as great as 0.02 second in the initial negativity over the ventricular surfaces, the order of excitation over the epicardial surface being the central ventral portion of the right ventricle, right base, right apex, left apex and left base (Fig. 5). According to these experiments, we may not regard the onset of ventricular contraction as involving the entire bulk of ventricular muscle fibers.

Variations in the Velocity of Transmission.—Under a variety of conditions the velocity of impulse propagation may be reduced or its spread may be entirely blocked. These influences have largely been studied in relation to conduction across the *A–V* node and bundle, but recent experiments (Lewis and associates, Meek and Eyster) indicate that they apply, also, to a different degree, to auricular conduction. Among the influences which have been found to retard conduction are: (*a*) Pressure, (*b*) cold, (*c*) certain chemicals and drugs, (*d*) interference with normal blood supply, (*e*) vagus nerve influences, and, finally, (*f*) too rapid a rate of excitation. The effect of all these influences, when mild, is to produce a delay in the transmission rate—when more marked, an occasional block, and when pronounced, a total block. Since most of these influences operate only under unnatural or pathological conditions, it may be questioned whether the rate of conduction from point to point varies a great deal normally.

Other Sino-ventricular Paths.—The probability that impulses reach the ventricle entirely and necessarily through the His-Tawara system is generally regarded as established by the fact that section of the bundle of His causes a dissociation of auricular and ventricular beats. A number of observations (Kronecker and Busch, Paukul) appear to contradict this conclusion, for these investigators found that ligation of the *A–V* bundle did not block impulses to the ventricle. Furthermore, Kent has described definite muscular paths running from the posterior auricular wall on the right side to the ventricular septum (right lateral connections), and has shown that proper auricular ventricular sequence may be maintained when all other connections were severed. Whatever the importance of these findings may be in rodents

and certain mammals, the fact remains that no such results can be demonstrated in the heart of the goat, dog, monkey or man. On the contrary, the His bundle is the only connection capable of transmitting impulses (Cohn and Trendelenburg). Finally, mention may be made of reports that the *A–V* bundle and its connections are apparently absent in some human hearts examined. The suggestion may be made that such failure is attributable to the fact that hearts were not obtained sufficiently early after death and that the tissue had undergone glycogenolysis.

Contractility and Irritability.—Cardiac tissue[1] possesses certain fundamental characteristics by virtue of which it differs in its responses from skeletal muscle. It has long been recognized that heart muscle responds by maximal contractions to all stimuli which are not subminimal (Bowditch), a reaction that has been designated as the *law of all or none.* This type of response may probably be attributed to the extensive intercommunication of the muscle syncitium rather than to any peculiarity of cardiac tissue *per se* (Lucas, Gotch). The practical significance of this phenomenon lies in the fact that the amplitude of cardiac contraction is in no wise determined by the intensity of the natural impulses which excite the muscle, but is solely dependent on the state of irritability at the time of stimulation. The cardiac irritability may, however, be affected in a variety of ways, and consequently the heart is able to respond to stimuli received with contractions of larger and smaller amplitude (*e. g.*, after repeated stimulation, chemical action, drugs, nerve influences, etc.). The factor which normally plays the greatest role in modifying the amplitude and duration of contractions through a change in irritability is the degree to which the muscle fibers are stretched. As this involves both a change in length and a change in the tension of the muscle fibers, the question has naturally arisen whether the *initial tension* or the *initial length* determines the response of cardiac muscle. Upon this question opinions are still divided, the observations of Frank, Straub and Wiggers indicating that initial tension determines the magnitude of response; those of Kozawa, Patterson, Piper and Starling supporting the view that initial length fundamentally determines the amplitude of contractions. Gesell interprets his experiments as indicating that either one may affect the amplitude of contractions without the other. According to most investigators (Straub, Wiggers and associates), stretching of cardiac muscle also increases the duration of the contraction process.

The Refractory Phase.—The reaction of cardiac muscle to stimuli differs according to whether it is excited during its contraction, relaxation or rest period. Stimuli applied early during relaxation evoke

[1] For experimental work relating to irritability and contractility of nodal and Purkinje tissue consult Erlanger, Am. Jour. Physiol., 1912, **30**, 395; Lewis, Quart. Jour. Med., 1921, **14**, 337; Wierisma, Arch. neerland. d. physiol., 1922, **7**, 543.

merely a small mechanical response; the later they are applied during relaxation the greater the amplitude becomes, and under certain conditions it may even exceed normal. If, on the other hand, a stimulus is applied during the process of contraction the heart responds neither with an augmented contraction, as does skeletal muscle, nor with a subsequent contraction during diastole. In other words, the heart is said to be in its *refractory phase* (Kronecker, Marey). This refractory stage is not strictly limited to the phase of contraction, however, for there is a short interval early in diastole during which minimal stimuli eliciting a contraction later in relaxation fail to cause a contraction. In other words, the nearer to the end of systole that a stimulus is applied, the stronger it must be in order to evoke another contraction. This interval, in which strong stimuli alone elicit a response, has been termed the *relative* or *variable refractory phase* in contradistinction to the *absolute refractory phase* occurring during contraction, in which no response can be elicited by stimuli of any magnitude (*cf.* Fig. 6). These peculiarities of cardiac muscle have been interpreted to indicate that early in relaxation a rearrangement of certain ions occurs in relation to colloid membranes within the muscles, and that, by virtue of such rearrangement, electrical energy is stored which expresses itself in terms of a muscle's ability to become excited. At the moment of reaction to a stimulus this energy is completely discharged and the muscle then fails to respond to any stimuli during the remainder of contraction because neither the chemical reaction nor physical rearrangement of ions in relation to colloidal particles has been completed (*cf.* Adrian, Schultz, Howell).

The rate at which irritability recovers during relaxation may be judged by noting the magnitude of response to effective stimuli applied during and after the relative refractory phase. If the stimulus falls during the relative refractory phase the contraction summit is not as high as normal; whereas, when applied after this phase the contraction summit may exceed normal (Bowditch). Recent work (Adrian, Wastl) indicates that during relaxation the irritability of heart muscle varies much as that of nerves, viz., the heart muscle passes through: (1) A period of reduced but rapidly increasing irritability (*i. e.*, during the relative refractory period), (2) a stage of supernormal excitability which gradually returns to (3) a stage of normal excitability. (For the interpretation of these phenomena, *cf.* Adrian, Mines.)

Various influences may operate to modify the duration of the absolute and relative refractory phases. Thus, it has been shown in the case of ventricular muscle that certain drugs (*e. g.*, chloral) may abridge or abolish the relative refractory phase altogether (Rohde, Schultz), while other drugs (Ba, digitalis, veratrine, quinidine) extend the duration of the absolute refractory period both in the auricle and ventricle (de Boer, Lewis and associates, Cohn and Levy).

Inasmuch as the hearts of crustaceæ, in which ganglion cells and nerve fibers are situated extracardially, do not exhibit a refractory period, the question has arisen whether the refractory state in vertebrate hearts is a function of the muscular tissue or of the ganglion cells contained within the muscle. The fact that the refractory period can be abolished (Rohde) or abridged (Schultz) by chloral hydrate would seem to favor the former view, especially since in the limulus heart this drug acts by preference on the nerve cells (Carlson). It may be pointed out, however, that the admission that nerve cells determine the refractory phase in no way compromises the view that the impulse is of myogenic origin.

Influences of a more strictly physiological order may, however, also affect the duration of the refractory phase. In the mammalian auricle vagus stimulation may reduce it (Lewis, Drury and Bulger). Of greater significance, however, is the relation of the refractory phase to the rate of excitation. The longer the interval between stimuli the longer the duration of systole and of the absolute refractory phase becomes both in the auricle and ventricle (Schultz, de Boer, Mines, Lewis, Drury and Bulger). Or, stated in another way, the more rapid the rate of stimulation the shorter the refractory phase becomes. Thus, Lewis, Drury and Bulger found the following refractory phases in mammalian auricular tissue at different rates of excitation:

Rate.	Refractory phase.
100	0.02
130–140	0.15–0.17
290	0.08–0.11

It is obvious that, by virtue of this shortening of the refractory phase, the muscle is able to respond to more rapid rates of excitation than would otherwise be possible, for as soon as stimuli are repeated at intervals which are shorter than the refractory phases, certain stimuli cannot evoke a response. When this critical rate is reached the cardiac responses in the case of the frog's ventricle drop abruptly to half that of the auricle (Mines, de Boer), *i. e.*, it adopts a form of *half-rhythm* or 2:1 *response*. The interval between stimuli, therefore, becomes a measure of the shortest refractory phases which that particular type of muscle can develop. The critical rate at which this half-rhythm develops varies in different animals and in the muscle tissue from different portions of the same heart. Thus, *half-response* occurs in mammalian auricular tissue at approximately 450 excitations per minute, for ventricle at the rate of 350 per minute and for nodal tissue between 270 and 300 per minute. Interpreted in other words, the refractory phase of auricular tissue is smallest, of nodal tissue greatest, while the ventricle occupies an intermediary position (Lewis).

In mammalian auricular tissue the change from complete response to a 2:1 response does not take place abruptly, however. The two

are separated by a period during which some stimuli are effective and others not. Thus, an auricle which responds to every stimulus up to 300 per minute may not develop a strict 2:1 rhythm until a rate of 450 per minute is reached. Between these rates there exists a phase in which at first large and small beats alternate, and later certain stimuli drop out in haphazard fashion. The phase of early diastolic relaxation where this takes place has been designated as the *partially refractory phase* (Lewis, Drury and Bulger) (*cf.* Fig. 6). This stage of irregular response is apparently due to the fact that all the fractions composing auricular tissue apparently do not have precisely the same minimal refractory phase and consequently fail to be excited at different excitation rates. Thus, we may suppose that at 350 excitations per second most of the fractions still react, but a few fail to do so

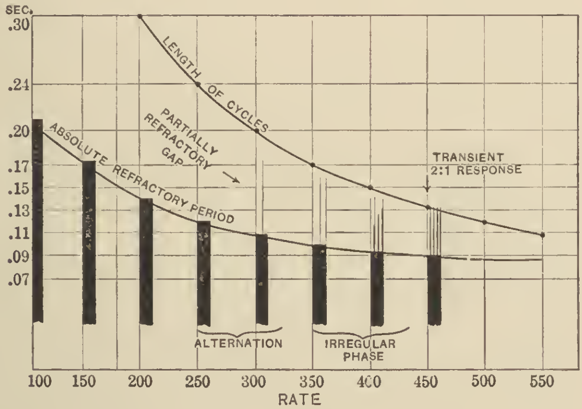

Fig. 6.—Diagram showing that absolute refractory period does not decrease in proportion to auricular cycle as rate increases. Also illustrating the development of the partially refractory phase and 2 : 1 response. (After Lewis, Drury and Bulger.)

because the excitation strikes them during their refractory phase. A condition then results in which some fibers react by a 1:1 response, others by a 2:1 response. As long as the number of refractory fibers is small the tissue, as a whole, still responds; when they increase slightly in number the tissue still responds but with a smaller beat, thus producing an *alternation* in the amplitude of consecutive beats. Further, as more and more refractory portions responding in 2:1 rhythm enter and the number of responsive fractions decreases, it is obvious that a stage will finally develop in which no appreciable reaction follows an occasional beat.

When, for any reason, the nutritive condition of a regularly stimulated heart is impaired, and the conduction of impulses is in consequence delayed, then the effect of a premature stimulus given in the responsive phase of the cycle depends on the time of its application.

Given some time after the end of the refractory phase, it induces a single extracontraction followed by a compensatory pause as in normal hearts. Applied a short time after the end of the refractory phase, it induces a series of extrasystoles. Finally, applied immediately after the end of the absolute refractory phase, it throws the ventricle into an apparently incoördinated state of contraction termed *fibrillation.* Thus, in a ventricle in a nutritively impaired state, whether a stimulus gives rise to a single extracontraction, to recurrent systoles or to fibrillation depends upon the time after the refractory period at which a stimulus is applied (de Boer).

In explanation of these phenomena it should be recalled that an extrasystole elicited early in diastole is not only small in amplitude but has a very short refractory phase. If, at the same time, the conduction rate is depressed there will be a tendency to establish a circuit of excitation and, in this manner, the ventricle reëxcites itself. In recurring extrasystoles conduction takes place evenly; in fibrillation unevenly. The bearing of these observations on clinical fibrillation both in the auricles and ventricles will be discussed later (*cf.* pages 474 and 489).

The Latent Period.—As in skeletal muscle, a short interval intervenes between the time of excitation and the onset of the mechanical response; as in skeletal muscle also we may suppose that this interval is apparent rather than fundamental, being largely due to the difficulty of registering the inception of mechanical changes. In spite of these handicaps, however, it has been found that the latent period of mechanical response is probably about 0.02 second in the mammalian auricle and 0.03 to 0.04 second in the ventricle. Garten and Weber found that the interval between the rise of P_{II} in the electrocardiogram and right intra-auricular pressure was only 0.01 to 0.022 second, while the intraventricular pressure rose from 0.017 to 0.021 second after the beginning of R_{II}. In reinvestigating these relations, Wiggers obtained similar figures for the delay in the rise of intra-auricular pressures (average, 0.022 second), but found somewhat longer intervals in the case of the intraventricular pressure rise (0.03 to 0.045 second). Comparisons of the initial vibrations of the first sound with the R_{II} wave of the electrocardiogram have shown similar time relations (Kahn, Bull, Lewis, Fahr, Battaerd).[1] By recording the contraction waves from two points on the auricular surface simultaneously with the arrival of negativity at these points, I have obtained results which indicate latent intervals ranging from 0.04 to 0.06 second. These intervals are somewhat longer than those obtained by Lewis, Feil and Stroud, who compared the electrical and mechanical changes of isolated points on the auricular surface (0.02 second; occasionally 0.05 second). The possible variations of these periods have not been extensively

[1] For details, see Chapters XV and XVI.

studied. The writer has observed that the latent period is apparently not altered when the auricle is beating at a rapid rate in flutter.[1]

Tonus.—Convincing experimental evidence has not yet been presented that tonus of the mammalian ventricle is capable of changing under conditions that may be considered physiological and that such changes are of importance in determining ventricular efficiency. The conception that cardiac tonus is capable of changing rests largely upon observations of the terrapin auricle, in which normal variations may not be contradicted (Fano, Botazzi, Gesell, Porter). We cannot be so certain, however, in regard to similar changes in the mammalian ventricle. The literature, it is true, is full of references to variations in diastolic length of the mammalian ventricle both perfused and *in situ;* but their bearing on the question of physiological tonus variation is doubtful, partly because the reactions usually follow the use of drugs or chemicals which are not natural, partly because the variations in diastolic length may more probably be assigned to influences other than tonus. Indeed, the study of tonus variations has unfortunately been complicated by the fact that the conception which *defines tonus as a state of sustained partial contraction by virtue of which the muscle resists stretching* has not been adhered to, and consequently it has not been generally recognized that *changes in diastolic length of ventricular muscle are no criterion of tonus change unless the duration of diastole and the distending pressure remain constant.* The difficulty in controlling these factors in intact hearts is indeed the reason why such changes in diastolic volume as are known to occur under physiological conditions may not be interpreted without great reserve as indicating tonus changes. (For further discussion, *cf.* pages 120, 412.)

Of the many influences which may affect ventricular tonus, the following may be regarded as physiological, viz.: (*a*) Influence of accelerator nerves; (*b*) variations in temperature within body ranges; (*c*) variations in O_2 and CO_2 content; and (*d*) variations in composition of nutrient media. The possible role that these factors play in modifying tonus may therefore be better studied on perfused hearts.

When rate changes do not take place during perfusion, as ordinarily performed by the methods of Martin or Langendorff and Schäfer, it is probable that variations of intraventricular pressure are fairly constant and that changes in length indicate tonus variations. Even such experiments should be checked more rigidly, however, as to significance of changes in diastolic length. It is precisely under such conditions, however, that tonus fluctuations do not, as a rule, occur spontaneously, *i. e.*, when the temperature is kept at body levels and the composition of the perfusion fluid is not altered. Many experimenters who have perfused extensive series of hearts will probably be able to testify to the fact that there are a few exceptions to

[1] Wiggers: Am. Jour. Physiol., 1922, **62**, 310.

this statement and a few reports of such variations have been made (Busquet and Tiffeneau, Porter). It must, nevertheless, be concluded, at the present state of our knowledge, that crucial proof is still lacking that the ventricle is endowed with that type of fundamental metabolism by virtue of which it is capable of altering its diastolic length under constant environment.

INFLUENCES DIRECTLY AFFECTING THE HEART BEAT.

The functions of the heart may be influenced not only through nervous channels, but also by thermal, mechanical and chemical influences brought into play through the blood stream. The manner in which these act has been investigated in two ways, viz., by the perfusion method and by means of the denervated heart.

The Perfusion Method.—The perfusion method offers a convenient method by which the factors may be separately varied and controlled with greater precision than is possible in the intact heart. In principle, perfusion aims to pass through the vessels of the heart a stream of nutrient fluid under normal conditions of temperature and pressure in such a manner that both ventricles are adequately supplied.

For general work the procedure first employed by Martin and later by Langendorff is usually employed. A cannula is placed in the aorta and, as the perfusion pressure closes the semilunar valves, the fluid enters the coronary vessels directly. The venous blood returns by the coronary veins, distends the right auricle and ventricle and is eliminated during each contraction from the pulmonary artery. As the initial intraventricular pressure probably does not vary appreciably under such conditions, accurate myograms from the right ventricle are probably fairly reliable indices of changes in systolic and diastolic lengths of the right ventricle.

The method has the disadvantage, however, that the left ventricle remains relatively empty and becomes rigidly contracted. To obviate this the method of Schäfer may be employed, which consists in pushing the cannula beyond the semilunar valves into the ventricle and thus distending it by the perfusion pressure, which should be somewhat lower than in the method of Langendorff. As the ventricle contracts, the fluid is forced around the cannula into the aorta and thus into the coronary system. By simultaneously registering the pressure within the left ventricle and changes in its length, the relations between initial pressure and initial length may be compared.

While these methods are adequate and, indeed, preferable for the study of specific influences affecting the fundamental contractions of the heart beat, it is necessary, in studying the problems of cardiodynamics, to supply the perfusion fluid to the various chambers of the heart in the same sequential order as occurs normally. For these purposes modifications of the heart-lung preparations originally

described by Martin are more suited (Gesell, Starling and associates, Straub). The forms of apparatus elaborated are so numerous and the choice of solutions so great that it would carry us beyond our scope to enlarge upon them.[1]

The Denervated Heart.—When both vagi nerves are divided and both stellate ganglia are excised, all known connections of the heart with the central nervous system are severed and consequently any changes in its action must result through physical, thermal or chemical changes in the blood stream. Such a preparation has been employed among others by Johansson, Guthrie and Pike, Gasser and Meek, Cannon. It has the advantage over the isolated and perfused heart in that its activity is not susceptible to alteration on account of imperfections in known perfusing fluids (*cf.* Belt, Smith and Whipple), and when one factor leads to another in disturbing the heart beat the resultant direct effects probably correspond more clearly to those obtaining in the body. It has a limitation not shared by the perfusion method—that the ultimate cause of changes produced by a variety of physiological influences cannot always be determined. Both methods, therefore, complement each other in elucidating the influences directly modifying the heart beat.

Effects of Temperature Changes on the Isolated Mammalian Heart.—An increase in temperature above 37° causes an increase in heart rate until an optimum temperature is reached. Beyond this the rate diminishes and at about 44° to 45° C. the beat ceases entirely (Martin). The rate decreases as the temperature falls and at temperatures ranging from 13° to 19° C. the beat ceases entirely. Rhythmicity in such cases remains latent, however, and, upon subsequent warming, a coördinated beat is reëstablished. Most observers have failed to find either a linear or logarithmic relationship between frequency and temperature changes in the mammalian heart (Clark, Frank, Snyder), and the linear relationship found by Knowlton and Starling is acknowledged by them to be, in all probability, accidental. Furthermore, the coefficient of alteration (*e. g.*, $\frac{\text{frequency at } 30°}{\text{frequency at } 20°}$) is also not a constant one (Clark). All that we can say, therefore, is that within physiological limits the heart rate varies in the same direction as temperature, but no definite law appears to control the rate of change. The change in the amplitude of contraction appar-

[1] For a description of various forms of apparatus, see Tigerstedt's Handbuch der Physiologischen Methodik, **2**, Part 4, 144. More recent forms of apparatus which have come to the author's attention are: Aducco (Arch. ital. de biol., 1916–1917, **66**, 137), Dresbach (Quart. Jour. Exp. Physiol., 1914, **8**, 73), Eyster and Loevenhart (Jour. Pharm. and Exper. Therap., 1913, **5**, 57), Gesell (Am. Jour. Physiol., 1916, **40**, 267) and Frölich and Pollak (Arch. f. d. ges. Physiol., 1920, **184**, 211). For studying contractions of isolated strips of heart muscle, see methods described by Clark (Jour. Physiol., 1920, **54**, 279), Eiger (Zentralbl. f. Physiol., 1918, **32**, 205), Erlanger (Am. Jour. Physiol., 1910, **27**, 87), Porter (Am. Jour. Physiol., 1898, **1**, 511) and Weekers (Arch. internat. de physiol., 1906, **4**, 76).

ently depends on the temperature ranges within which they occur. Personal observations indicate that between the approximate ranges of 35° to 39° the amplitude of ventricular contraction generally increases as the temperature and rate increase. Clark, however, found that the contraction of auricular strips always decreased in amplitude. At temperature above this range ventricular amplitude decreases and at lower temperature it increases (Langendorff, Patterson, Piper and Starling, Eckstein). It is impossible to state at present to what extent this is due to a primary effect on contraction and to what extent it is due to associated changes in heart rate.

Furthermore, it is necessary to bear in mind that amplitude of contraction is not an index of a heart's ability to perform work (*cf.* page 136), but that this can only be estimated when the heart contracts isometrically. While this cannot be done on mammalian hearts, the work of Patterson, Piper and Starling indicates that in the mammalian ventricle, as in the skeletal muscle and the frog's ventricle (Doi), the power of performing work at equivalent initial lengths is greater at lower temperatures; in other words, the heart economizes energy better at lower temperatures.

Warming increases the diastolic length, but cooling decreases it; but, again, it does not appear to have been clearly demonstrated whether this is due to changes in tonus or dependent upon variations in heart rate. The duration of the contraction is lengthened as the temperature falls. This is shown to an astonishing degree in the experiments of Langendorff, who found changes in contraction values from 0.13 second to 10 or 12 seconds when the temperature varied from 44° to 10° C. Similar but of course much smaller changes are shown when variations of 5° or 6° occur within physiological ranges (Patterson, Piper and Starling). The duration of the refractory phase changes with that of systole (Eckstein). As such changes are apparently greater than can be accounted for by the slowing of the heart rate at low temperatures, it must be concluded that the velocity of the physicochemical reactions concerned in irritability and contraction are themselves determined by temperature changes.

Heat is said to augment and cold to depress the rate of conductivity from auricle to ventricle. Experiments in which *A–V* conduction is facilitated by the local application of heat to the *A–V* node indicate that the effects of general temperature changes on conduction must probably be referred to its effects on this structure. While it has been established that the conduction rate to ventricular muscle is always facilitated in the frog's heart (Clark), these observations do not seem to have been as yet extended to conduction in mammalian auricular and ventricular tissue.

Effect of Coronary and Intraventricular Pressures.—In general, the coronary pressure determines the volume of blood flowing through the coronary vessels. While fairly vigorous contractions may be

maintained on a very small blood supply (Porter), there is a lower limit below which the amplitude of contraction and the power of performing work under stress is adversely affected (Knowlton and Starling). An increase in coronary pressure, as determined by arterial pressure in the aorta, tends to cause somewhat larger and steeper contractions. According to the records and charts published by Prince, the duration of the contraction phase is also slightly abbreviated, but neither the rate of relaxation nor its duration is in any way affected by changes in coronary pressure as has often been supposed. It is doubtful, however, whether the improved action of the heart is entirely dependent upon the increased volume of blood supplied by a sufficient coronary pressure. On the contrary, it appears that it is in part attributable to the intravascular pressure itself, for an adequate beat of the heart may be maintained for a short while when its vessels are perfused either with indifferent gases (Magnus) or with neutral oil (Sollmann). Finally, it must be mentioned that changes in coronary pressure are apparently without effect on the rate of a normally beating heart (Magrath and Kennedy, MacWilliam, Lehndorff, Knowlton and Starling), an effect that may be interpreted as due to the fact that the thin-walled auricular tissue receives its nutrient supply largely from the cavity of the auricle and not to any great extent from the coronary tributaries.

Porter and his pupils were probably the first to show that an increased intraventricular tension causes an increase in the contraction amplitude of the mammalian heart in spite of the fact that this decreases coronary flow. The effects of initial tension are, therefore, apparently more important than vascular supply in determining contraction amplitude. Under the influence of stretching the amplitude of contraction not only increases (within limits), but the duration of its contraction phase is also prolonged (Straub). The optimum intraventricular tension at which maximum beats occur varies, of course, in different perfused hearts. According to Henderson and Prince, the optimum initial tension for the cat's heart is 50 mm. of saline for the right ventricle and 150 mm. for the left. Straub, as well as Patterson, Piper and Starling, found increased responsiveness above these figures, however.

Effect of Composition of the Perfusion Fluid.—A historical survey of the various fluids used to maintain the perfused heart gives an insight into the constituents which are absolutely essential to maintain its beat. In the earliest experiments defibrinated blood diluted with equal volumes of isotonic saline was used and found to satisfactorily maintain the heart beat. When defibrinated blood is replaced by serum the beat is not maintained unless the serum is charged with oxygen under pressure (Porter), indicating the absolute necessity of oxygen for the maintenance of irritability. That oxygen is not the only requirement for the heart to continue beating can be readily

demonstrated by perfusing it with an oxygenated isotonic sodium chloride solution. The beat promptly ceases (Kronecker and Starling).

The question then arises: What other constituents are essential to the heart beat? Naturally the idea first suggested itself that "nutritive blood proteins" were necessary, a view which apparently received confirmation when it was shown that the addition of various proteins (blood proteins, egg proteins or milk proteins) to an oxygenated saline solution favored or restored the beat (Kronecker). This view became less probable again when it was found that the proteins could be replaced entirely by a nonprotein substance, such as gum-arabic. Hence, it was believed that the proteins exerted no nutritive function, but that they favored the beat by virtue of the viscosity which they imparted to the solution (Albanese). Subsequently, it was also shown that the proteins are not utilized by the beating heart (Howell and Cooke). The same is true of amino-acids. Thus, experimental work makes it extremely probable that, instead of being absorbed, such amino-acids as alanine, glycocoll and tyrosine are actually washed out of the heart (Buglia, Tsuji, Wishart and Wiggers[1]).

It has long been known (Ringer) that the frog's heart can beat on an inorganic mixture which contains sodium, calcium and potassium, while the beat is very much improved by the further addition of sodium bicarbonate. It was but a step to show that upon an oxygenated Ringer's solution the mammalian heart executes rhythmic beats. The store of energy-yielding material in the heart must be restricted, however, for the effect of such a solution extends over only a short interval of time. By adding glucose as an available form of energy, Locke found that the heart perfused with Ringer's solution improved. That glucose is actually metabolized by the beating heart has been abundantly demonstrated, not only by the fact that glucose disappears from the perfusion fluid (Locke and Rosenheim), but also by the fact that lactic acid (Tsuji) and CO_2 (Evans, Rohde) are liberated in its metabolism.

Summing up the evidence, it appears that when sodium, calcium and potassium are present in balanced proportions in a solution which

[1] The unpublished work which is referred to in this reference was carried out in 1914. Hearts were perfused by a closed-system method with Locke's solution to which varying quantities of alanine and glycocoll were added. Analysis of a perfusion fluid indicated that the percentage of amino-acids increased rather than decreased after one or two hours' perfusion. Since the total volume of water decreased, partly through edema of the heart, partly through a possible slight evaporation, we felt that these results indicated a probable rather than a quite certain evidence that amino-acids were washed out of the heart. The investigation was continued therefore by estimating the amino-acids' content of portions of the heart muscle before and after perfusion. The results again showed definite reductions in the amino-acid content of heart muscle. Inasmuch, however, as we saw the possibility of a technical error in the method employed, it was deemed desirable not to publish an extensive report of this investigation. We feel inclined to regard this as giving suggestive, though not absolutely conclusive, proof of our statements. Other investigators, however, do not seem to have had any scruples in accepting a reduction in amino-acid content in the perfusion fluid as evidence of its being washed out.

also contains some alkali and oxygen, the heart is capable of beating, while the further addition of glucose maintains the beat for many hours or even days.

The demonstration that the mammalian heart can beat on such a simple mixture of salts, naturally led to more detailed investigations of the single necessary elements.[1]

Role of Salts.—Calcium, in proper proportions, is absolutely necessary to the beat of the heart. In excess it causes an increased tonus, which may become so extreme as to entirely prevent the fundamental contractions. Similar tonic contractions are produced by small quantities of the other alkaline earths (barium, strontium, etc.). Potassium ions are apparently not absolutely necessary to rhythmicity, hearts having been made to beat on perfusion with a mixture of sodium and calcium ions alone. When present, however, potassium favors relaxation and tends to reduce the irritability to artificial stimuli. In excess it causes the heart to stop in extreme relaxation.

The study of the role played by potassium has in recent years been especially investigated in the frog's heart. Apparently potassium may be replaced by a number of other metals. In connection with this substitution considerable interest attaches to the experimental work initiated by Zwaardemaker and his associates, which suggests that potassium acts, not by virtue of its ionic antagonism to calcium, but rather because of its radioactivity.[2]

The experimental facts so far established may be briefly summarized: A frog's heart in diastolic standstill, as a result of perfusion with a potassium-free solution, may be revived by the substitution of radioactive metals. This has been accomplished not only by substances which, like potassium, emit beta rays (*e. g.*, cesium and rubidium), but also by a large number of substances emitting alpha rays (*e. g.*, thorium, uranium and ionium). In substantiation of the idea that these substances act by virtue of radioactivity rather than as substituted ions, the following facts may be quoted:

1. In order to produce a revival of beats after potassium standstill, these substances must be present, not in molecular proportions as regards the normal potassium constituents, but in radio-equivalent amounts (Zwaardemaker).

2. The beat may be restored by colloidal forms of these metals, *e. g.*, by colloidal ionium hydroxide (Levend).

3. Emanations from radioactive fluids and radiation by radium or mesothorium rays act in the same manner as the addition of radioactive substances to the solution in restoring the beat (Zwaardemaker and Feenstra, Zwaardemaker and Grijns).

[1] For a comprehensive review, see Tigerstedt: Physiologie des Kreislaufes, Berlin and Leipzig, 2d edition, 1921, **1**, 245.

[2] For the technic of studying radioactive substances and data as to radioactive equivalents, see Zwaardemaker: Arch. neerlandaises de physiologie, 1921, **5**, 285.

At present indications are that while alpha active substances are capable of reviving a heart brought to a standstill by lack of potassium they cannot entirely replace potassium which emits beta rays. Thus, if a heart beating as a result of the addition of uranium is subsequently perfused by a solution containing potassium, it ceases promptly, indicating a radioactive antagonism (Zwaardemaker). Furthermore, the hearts beating as a result of potassium and uranium are not equivalent as regards their physiological reactions to stimuli (*cf.* de Boer).

Although most of these observations have been made on the hearts of amphibia and reptiles, they may with reasonable certainty be assumed to apply to mammalian hearts. Indeed, it has already been shown that the substitution of uranium for potassium has identical effects on the perfused mammalian heart (Jannink and Feenstra).

As to the importance of other inorganic substances normally found in blood serum, notably magnesium and the phosphates, comparatively little evidence of a positive influence is available. Most investigators are agreed that the addition of magnesium to the perfusion fluid exerts no pronounced effects, while the advantage of the phosphates probably lies in the fact that by their presence the buffer action of solutions is improved. On the grounds that a fluid containing all inorganic constituents of the blood is more favorable for cardiac action, a number of different perfusion fluids have been suggested. The following table summarizes their composition expressed in grams per liter:

TABLE SHOWING COMPOSITION OF PERFUSION FLUIDS.

	Locke.	Adler.	Tyrode.	Göthlin.	Clark.
$NaCl$	9.00	5.90	8.00	6.50	6.50
KCl	0.24	0.40	0.20	0.10	0.14
$CaCl_2$	0.42	0.40	0.20	0.065	0.12
$MgCl_2$	..	0.25	0.10		
NaH_2PO_4	..	0.126	0.05	0.008	0.01
Na_2HPO_4	..	..	..	0.009	
$NaHCO_3$	0.1–0.3	3.50	1.00	1.00	1.00
Glucose	1.00	1.50	1.00	1.00	2.00

Influence of the Reaction of the Perfusate.—The addition of small quantities of alkali to the perfusion fluid is apparently essential in order to maintain the cardiac beat. As this has long been regarded as necessary to neutralize CO_2 or fixed acids generated during muscular activity, the addition of Na_2CO_3, $NaHCO_3$ or $NaOH$ has generally been regarded as equally efficacious (Gross). More recent work, however, indicates that other alkalies may not be substituted for $NaHCO_3$ with impunity. When this is done to the rigid exclusion of all bicarbonates the rhythmic function of the *A–V* node is apparently lost (Mansfeld and Szent-Györgyi), while, according to Locke, this is a factor responsible for the firm state of contraction developing in the left ventricle.

Expressing the reactions of fluids in terms of H-ion concentration, it may be said that their composition may be so varied that they have

at the onset a pH very nearly equal to that of the blood. As ordinarily prepared from laboratory chemicals of theoretical purity only, wide variations in the pH of prepared solutions may obtain and these values may be further modified during the course of experiments (Boehm). Thus, Rona and Wilenko found that the pH of Locke's solution varied from 7.78 to 7.04 during his experiments, while Tyrode's solution had a more constant pH of 8.29. Experimental work indicates, however, that the frog's heart is capable of *maintaining a beat* within wide ranges in H-ion concentration (pH 7 to 12, Burridge; pH 2 to 12, Mines), the optimal ranges lying between pH 8.3 to pH 6.5 (Clark). Apparently, however, the optimal concentrations vary somewhat for different portions of the heart (Mines). The mammalian heart appears to work best when H and OH ions are very nearly balanced or when pH is slightly to the side of alkalinity, although markedly alkaline and weakly acid solutions both maintain the beat (Borrino and Vialo).

Very slight changes in pH may, however, modify both the rate and amplitude of contraction, as studied in amphibian hearts. Within the ranges of pH variations possible within the blood, a slight increase in alkalinity (pH 7.4 to pH 7.6) augments the tonus of the auricle and decreases the amplitude of contraction; a slight decrease (pH 7.4 to pH 7.3) produces reverse effects (Andrus). Closely related to changes in pH is the question of the effect of CO_2 concentration. Jerusalem and Starling found that blood exposed to 5 to 8 per cent CO_2 had a beneficial action. Ketcham, King and Hooker, on the other hand, report that 3 per cent CO_2 in solutions is deleterious to mammalian hearts. Mines has attempted to reconcile these contrary results on the basis that the perfusate of Jerusalem and Starling was too alkaline, and attributes the beneficial action due to slight increase of pH to a level near the optimum. He showed that a heart perfused with a solution pH 10.2 was benefited by the addition of CO_2, but that simultaneously the pH increased to 6.9. If, however, a solution with pH 7 were used for perfusion CO_2 had only a depressant effect. Clark also reported beneficial results when the pH was raised from 8.3 to 6.7 by increasing the CO_2 of the perfusing fluid, but assigns them to specific effects of CO_2.

Influence of Organic Constituents.—The activity of the heart is apparently increased by the addition of various nitrogenous extractives; for example, by small doses of urea, by ammonium carbonate, creatin, xanthin, hypoxanthin, sodium urate, etc. (Eyster, Backman). Similar effects have been obtained by small doses of indol and skatol (Danilewsky). Alanine and glycine, in the writer's experience, have no effect on a vigorously beating perfused heart, but according to Lussana, Hasegawa and Tsuji, they may, under certain conditions at least, increase both the rate and amplitude.[1] Cannon and Griffith

[1] According to Clark, the possibility must be considered that glycine may owe its favorable effect to the fact that it combines both CO_2 and K and, therefore, leaves Ca in excess.

tested a large series of amino-acids and found most of them without effect on the rate of the denervated heart. Tyrosine, however may, and tyramine (closely related chemically to adrenalin) regularly accelerates the denervated heart. Marked stimulating effects have been reported as a result of Witte's peptone (Popielski) and histamine (Einis). Proteoses derived from digested edestin, ovalbumin and casein, on the other hand, seem to depress cats' hearts (Gibson and Schultz). Foreign proteins and foreign sera exert a depressant and toxic action (Demel, Friedberger and Mita, Manwaring, Meinhard and Denhart, Leyton and Sowton). Such results obtained on perfused hearts should be applied cautiously to anaphylactic questions. Cushny and Gunn have shown that the same reaction follows when the serum from the same animal is added to the saline perfusion fluid, the preliminary augmented and accelerated contractions being followed by a stage of slowing and depression during which heart-block frequently occurred. The results are interpreted to mean that the heart perfused with Ringer's solution represents a hypodynamic organ rather than that the sera have a toxic action. More recent work indicates that the depressant activity of serum is not a fundamental effect on cardiac muscle, but is due rather to the intense vasoconstriction which it produces (Clark), for when serum is added to the saline solution bathing auricular strips it causes only slight increases in the rate and amplitude of contractions.

The addition of bile is reported to slow the rhythm, augment the tonus and diminish the expansion of the heart (Berti-Malesani); extracts of tissue organs (brains, nerves, etc.) depress the rate and amplitude of cardiac contraction either because of their cholin content or because they contain a large amount of potassium (MacLeod). Lecithin and, to a less degree, cholesterin tend to stimulate the heart, but may depress in larger doses (Danilewsky, Lawrow and Woronzow, Clark). Of the internal secretions, which are presumably found in the normal blood in small quantities, the actions of epinephrin and pituitrin are best known. Epinephrin or adrenalin, the active principle extracted from the suprarenal gland, causes an increase in the rate and amplitude of the perfused heart, the tonus being reduced. Pituitary extracts have the reverse effect; they slow the heart, decrease the amplitude and increase the tonus. Insulin, the internal secretion of the pancreas appears to have no effect on the perfused heart (Hepburn and Latchford.)

THE INFLUENCE OF THE CARDIAC NERVES.

Anatomical and Histological.—The heart is supplied by two sets of nerve fibers, those passing from the medulla[1] in the vagus trunk and

[1] Both histologic and physiologic investigations appear to indicate that the vagus fibers destined to control the heart arise from the dorsal vagus nucleus (Van Gehuchten and Molhant; Miller and Bowman).

those arising from the upper segments of the thoracic cord to pass by white rami fibers to the stellate ganglion, thence by the fibers of the

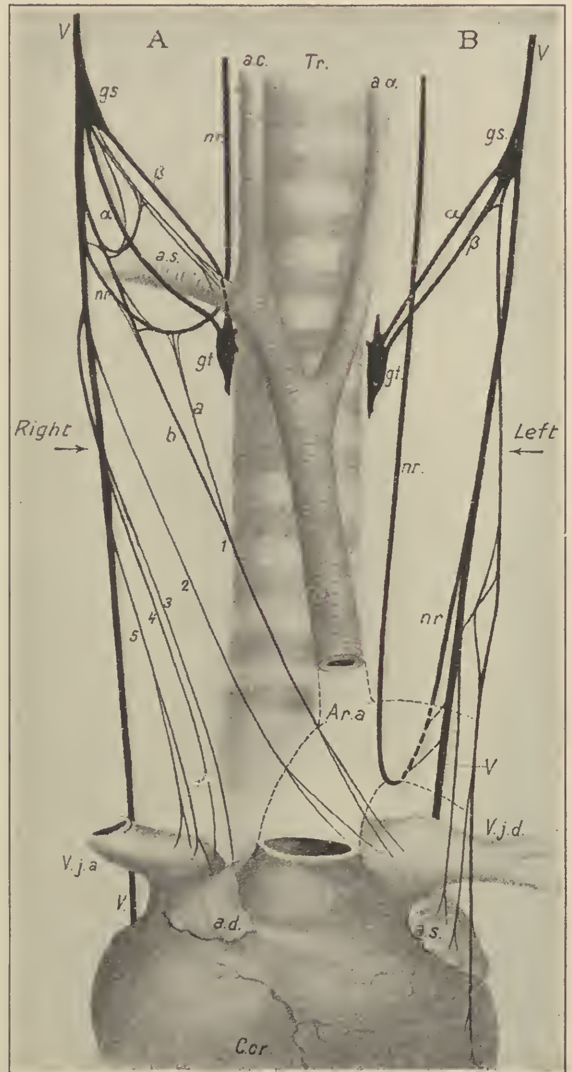

FIG. 7.—Nerve supply of the dog's heart. *v*, vagus nerve; *gs*, inferior cervical ganglion; *a*, *β*, annulus of Vieussens; *gt*, superior thoracic or stellate ganglion; *nr*, recurrent laryngeal nerve; 1, 2, 3, 4 and 5, vago-sympathetic filaments to heart. (After Dogiel.)

annulus of Vieussens to the inferior cervical ganglion, from which point fibers intermingle with those of the vagus in complex fashion. Fig. 7 shows the details as found in the dog, in which animal the rela-

tions resemble those in man (Dogiel). By special treatment the nerve fibers can be seen to form plexuses about the larger arteries and on the posterior surface of the auricles, some sweeping over the auriculo-ventricular groove to the ventricles. Between the fibers knob-like masses are everywhere evident in the basal plexuses of the heart (Boehm, Lim Boon Keng, Dogiel, Müller, Marchand and Meyer, etc.). The nerve supply is essentially homolateral, although there is some overlapping of the right fibers on the anterior aspect of the ventricle.

The most interesting question in connection with the nerve supply has been the relation of the extracardiac fibers to the fibers of the *S–A* node, the *A–V* node and the His bundle, with its branches. Although many technical difficulties have prevented histologists from actually following the connections, the relation is becoming gradually clearer as a result of the studies of Dogiel, De Witt, Keith and Flack, Meiklejohn, Morison, Oppenheimer and Oppenheimer, Wilson, Marchand and Meyer. The vago-sympathetic strands, which pass subepicardially to the posterior region of the auricle, apparently end around the multipolar and monopolar cells situated in the sinus region or on those in the interauricular septum. That they are truly relay stations for vagus impulses is evident from the fact that local application of nicotine abolishes the inhibitory vagus action (Marchand and Meyer). The ganglion cells around which medullated fibers presumably of vagus origin end are small. They contain many processes and their nonmedullated axones can be traced to muscle cells (Dogiel). The relation of another type of ganglion cell which is larger and ends in a long medullated axone has not been discovered. Within the sinus node itself ganglion cells are absent or very scarce, but nerve fibers, sometimes aggregated into a small nerve trunk, enter the sinus node from above and divide into delicate plexuses from which varicose fibers *terminate in simple or complex fashion around the nuclei of the muscle cells*. Similarly, fibers from the ganglion cells of the interauricular septum enter the *A–V* node and pass in bundles and plexuses into the ramifications of the His-Tawara system (Fig. 4). Some of these fibrils end around nuclei of the muscle cells while the termination of others apparently remains unknown. It is impossible from histological evidence to decide whether fibers passing to the ventricle outside of the *A–V* bundle belong to the sympathetic or the vagus system.

Action of Vagus and Sympathetic Fibers.—The vagus and sympathetic fibers exert an antagonistic action on the functions of the heart. Thus, as is well known, stimulation of the vagus decreases the rate while stimulation of the sympathetic accelerates it. This antagonism is generally regarded as not restricted to the effect on rate alone, but the vagus is supposed to exert a negative and the sympathetic a positive influence on all the functions of the heart. Moreover, according

to some investigators these functions are mediated by separate nerve fibers (Pawlow).[1] It will be our purpose to investigate to what extent these statements apply to different portions of the heart and their separate functions:

1. **Influence on Rhythmicity and Conductivity (Chronotropic and Dromotropic Effects.**—It is well known that if the divided vagus is stimulated by a weak tetanizing current the heart rate is slowed and the *As–Vs* interval is generally increased. If the stimulus is stronger the heart may be entirely stopped for a time, but eventually either the auricle or the ventricle, separately or both together, break away from the inhibition.

While it has long been known that the right vagus frequently exerts a more pronounced slowing of the ventricles, it has more recently been shown that a qualitative difference occurs as well (Cohn, Rothberger and Winterberg, Ganter and Zahn). Thus, when slowing of the heart occurs from stimulation of the right vagus no alteration in the conduction time may be apparent either from the *As–Vs* interval of myograms or from the *P–R* interval of the electrocardiogram. The suggestion that this indicates a direct influence of the vagus on the sinus node was further substantiated by Ganter and Zahn, who found that if during stimulation the node was warmed the normal rate was restored. Stimulation of the left vagus, on the other hand, usually causes a marked slowing of the ventricles without a corresponding change in auricular rate. Similar differences have also been observed in man as a result of compressing the vagi nerves in the neck (Robinson and Draper, Kleeman, Laslett). Although these changes are not manifest in all animals, such observations suggest that in the majority of cases the right vagus fibers communicate largely with the ganglion cells, sending fibers to the *S–A* node, while the left vagus fibers terminate chiefly around cells, the fibers of which are distributed to the *A–V* node and the His bundle (Fig. 4). In functional terms, this implies that the right vagus nerve exerts its greatest effect on rhythm production in the *S–A* node, while the left vagus is more essentially concerned with causing alterations in the *A–V* conduction. More recent experiments, however, make it improbable that this selective action of the two nerves is as marked as originally supposed (Bachmann, Meek and Eyster, Schlomovitz, Eyster and Meek, Lewis). It is, therefore, probably more correct to state that while the right vagus exerts a greater inhibition on impulse initiation in the *S–A* node of mammalian hearts, the left vagus also has a distinct effect on the rhythm production, while the left vagus has only a slightly predominant influence on the *A–V* node and bundle.[2] According to these results,

[1] For a review of early work, consult Hofmann: Nägel's Handbuch der Physiol. des Menchen, 1905, **1**, 260.

[2] For additional discussion as to the vagus effects on the terrapin heart, see Cruickshank (Am. Jour. Physiol., 1920, **54**, 217), Dale and Mines (Jour. Physiol., 1913, **46**, 319), Garrey (Am. Jour. Physiol., 1911, **28**, 330; 1912, **30**, 451), Gault (Ibid., 1917, **43**, 22) and Mines (Jour. Physiol., 1914, **47**, 419).

the fact that the right vagus usually produces no A–V dissociation must be explained in another way. Thus, we may suppose that both nerves depress A–V conductivity in the sense that the recovery of irritability after passage of an impulse is delayed. The reason that all impulses pass when the right vagus is stimulated and fail to pass when the left vagus is excited, may then be due to the fact that in the former case the rate of impulse delivery is so reduced that complete recovery in conduction is possible, while in the latter case the rate of impulse delivery is not sufficiently reduced, and, consequently, the A–V tissue is refractory at the time of the arrival, usually of alternate impulses. That this is the chief factor concerned in the block produced by moderate stimulation of the left vagus is evidenced by the fact that when the auricular rate is artificially kept constant, stimulation of the left nerve has only a slightly greater effect on A–V conductivity than does that of the right.[1]

When vagus stimulation causes a slower rate of the auricular beats this may be due, not only to a depression of the head of the S–A node which is the normal pacemaker, but occasionally this portion of the node may become entirely quiescent and the pacemaker transferred either to its lower end, to the coronary portion of the A–V node or to the ventricular portion. In the latter case a nodal rhythm with reversed ventricular and auricular beats takes place (Schlomovitz, Eyster and Meek). This indicates that the vagus produces its chronotropic effect on the heart by causing the seat of impulse initiation to move progressively to regions of lower automaticity.

When the coronary sinus portion of the A–V node becomes the permant pacemaker, after excision of the S–A node, the vagus also exerts a chronotropic effect but when the ventricular portion dominates the rhythm, little effect is evident (Eyster and Meek.)

The depressant influence of the vagi nerves on the rhythmic functions of the A–V node can be studied after the induction of nodal rhythm (*i. e.*, by depression or destruction of the S–A node (*cf.* page 29). In such cases stimulation of the left vagus (Meek and Eyster) and, according to Lewis, also that of the right causes the pacemaker to shift to another portion of the A–V node, or, in case the S–A node is not destroyed, it may be transferred back to this.

When the left vagus (rarely the right) is stimulated with strong currents a complete block of impulses across the A–V tissues may occur. When the ventricle "escapes" from such an inhibition and establishes a rhythm of its own the impulses may originate in the main bundle or in one of its branches; in the latter case one ventricular beat preceding the other. Again, we have evidence that the blocking effect may apply to one bundle more than another.

It is apparent, therefore, that the influence exerted by the vagi nerves on the functions of rhythmicity and conductivity is not only

[1] Removal of intra-auricular block by vagus stimulation has recently been reported by Lewis and associates (Jour. Physiol. (Proc.), 1922, **56**, ix).

exceedingly complex, but very variable in different animals. In general, however, it may be said: (1) That the magnitude of the influence of both nerves on nodal tissue decreases as these are traced downward, and (2) that the gradient of the left vagus influence is, on the whole, of a lower order than that of the right.

Stimulation of the right stellate ganglion causes an increase in auricular and ventricular rhythm without a change in conduction time. Upon stimulating the left stellate ganglion the heart not only accelerates, but the auriculo-ventricular conduction time is reduced or rendered negative (Hering, Rothberger and Winterberg), suggesting that the nerve terminals end around the *A–V* node and by increasing its irritability make this the pacemaker of the heart. If now the right stellate ganglion is stimulated a further increase in rate occurs, owing to the generation of more frequent impulses at the *S–A* node. So far no experimental observations have been made which question the interpretation that the right accelerator nerve chiefly affects the *S–A* node and the left accelerator nerve the *A–V* node.

2. **Influence on Irritability and Contractility (Bathmotropic and Inotropic Effects.**—It is frequently found that stimulation of the vagus diminishes the recorded contraction of the mammalian auricle (MacWilliam; Wiggers; and Lewis, Feil and Stroud), although the ventricular contraction usually augments, due to the long intervening rest. As the diminution in amplitude occurs also when the auricular rate is kept constant, the conclusion can only be reached that in the auricle at least the function of contractility is depressed by vagus stimulation (Fig. 8). According to Lewis and his associates, the duration of contraction as well as the refractory phase are also reduced. The former observation was not corroborated in optical myograms reported by the author (Fig. 8). The irritability of auricular tissue is likewise slowly decreased (MacWilliam, Wiggers) as vagus stimulation continues, for when the auricle is regularly responding to minimal artificial stimuli and the vagus is stimulated it fails after a while to respond to them (Fig. 9). These vagus effects are apparently shared by both nerves.

Stimulation of the sympathetic is said to cause, coincident with or apart from an acceleration, an augmentation of the auricular and ventricular amplitude (Pawlow); hence, it is generally assumed that the sympathetic contains augmentor as well as accelerator fibers.

All recent work seems to indicate that a direct vagus influence is not exerted upon the irritability or the contractility of the mammalian ventricle, for, aside from fibers distributed to the conducting system, the bulk of ventricular musculature probably receives no fibers in communication with the vagus (*cf.* Cullis and Tribe for literature). Since it is possible, however, to influence the amplitude of ventricular contraction even after the *A–V* node has been severed, the conclusion seems probable that the irritability and contractility of the ventricle may be influenced through the sympathetie fibers passing from auricle

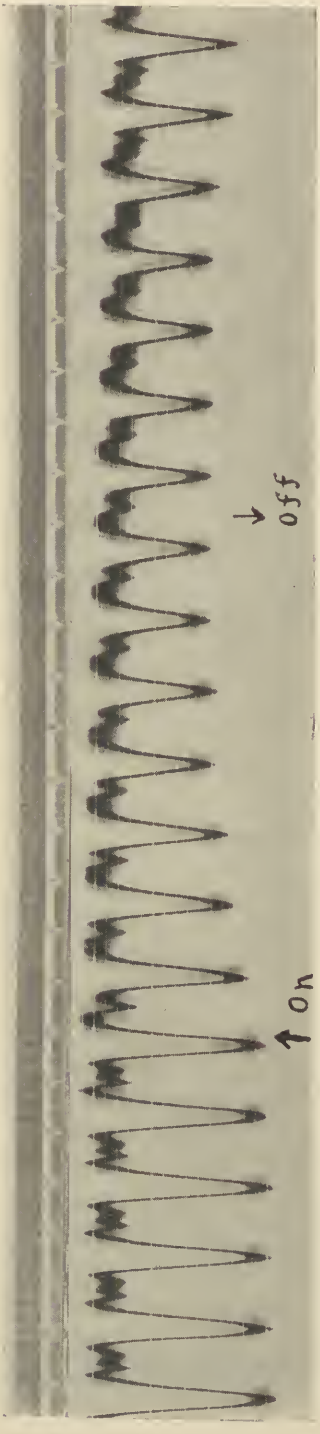

FIG. 8.—Optically recorded myocardiograms of auricle showing progressive depressant effect of vagus on amplitude and slow recovery after cessation of stimulation. Auricular rate kept constant by artificial stimuli—systole, downstroke.

FIG. 9.—Optical auricular myocardiogram showing depression of auricular irritability by vagus stimulation. Rate before stimulation kept constant by rhythmical application of *minimal* artificial stimuli. During vagus excitation amplitude first decreases without change in rate as in Fig. 8; later (beats x) artificial stimuli become subminimal and the natural slower rhythm dominates.

to ventricle outside the bundle of His. From studies on the hearts of cats, Henderson concluded that no augmentor effect is obtained except when the ventricle is beating with considerably diminished vigor and the arterial pressure is low. Even then he found it to be of little consequence, incapable of causing a stroke that more than compensated for the abbreviated diastole caused by the more rapid rate.

What seems to be certain evidence that the accelerator nerves exert a specific influence on ventricular contractions has been adduced, however (Wiggers and Katz), for by no other influence can the duration of ventricular contraction be so greatly reduced in relation to cycle length as by stimulation of these nerves or by the use of drugs exciting their terminals (epinephrin).

These facts are illustrated by comparing the actual $\frac{\text{systole}}{\text{cycle}}$ or *s/c*

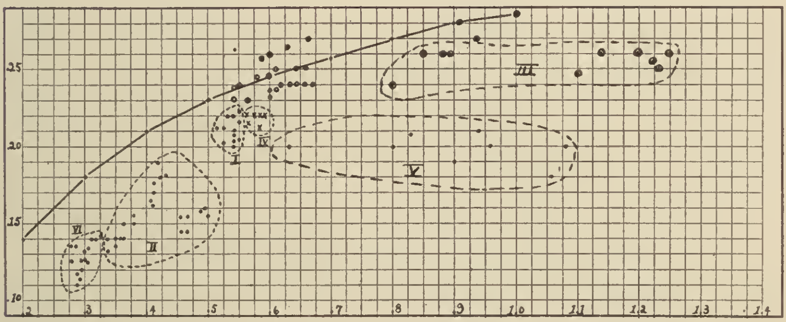

Fig. 10.—Plot showing the relation of actual $\frac{\text{systole}}{\text{diastole}}$ ratios obtained during accelerator nerve stimulation (Groups I, II, IV, V, VI) to the theoretical or calculated ratios shown as a curve. Abscissae, cycle lengths; ordinates, systole in tenths of a second. Detailed description in text. (After Wiggers and Katz.)

ratios at various heart rates with the theoretical values normal to each particular animal. Thus, in the experiment in Fig. 10 the line curve represents the theoretical *s/c* ratios as worked out from a stabilized vagal beat having a cycle length of 0.98 second and a systole length of 0.285 second. The small circles arranging themselves around the theoretical line are normal cycles representative of 40 measured beats. The large dots represent ratios occurring during vagus excitation. The small dots of Group I indicate the duration of systole during mild stimulation of the stellate ganglion; those of Group II, the effect of exciting the ganglion with a stronger current. In both instances the vagus nerves were intact. The crosses of Group IV represent the systoles of eighteen measured cycles after the vagi nerves had been cut and the accelerator nerves were acting alone. It is evident that a reduction of *s/c* ratios below the theoretical value occurs. In order

to determine the effect of accelerator stimulation on the *s/c* ratio when cycles of longer duration occurred, the effect of simultaneous stimulation of the accelerator and vagus nerves was tested. The dotted circles of Group III, arranging themselves somewhat below the theoretical line, show the duration of systole during such vagus slowing.

While the heart rate remained slow, due to vagus stimulation, the stellate ganglion was simultaneously stimulated. Although this caused some increase in rate, it did not equal that natural to the animal. The *s/c* ratio, however, decreased not only far below the theoretical ratios for such cycles, but also far below the *s/c* ratios of other much shorter cycles. This is evident on comparing the dots of Group V, representing nine measurements of beats occurring during simultaneous accelerator and vagus nerve stimulation, either with the dots of Group I, with the crosses of Group IV, or with the circles representing normal *s/c* ratios. Finally, after the vagi had been divided and *s/c* ratios represented by the crosses of Group IV had been attained, the stellate ganglion was again stimulated. The results of twenty-seven measurements are shown by the dots of Group VI.

These results indicate clearly that the *s/c* ratio is much reduced below the theoretical expectations by the influence of the accelerator nerves, not only at rapid, but at slower heart rates as well.

THEORIES AS TO THE CAUSE AND THE ULTIMATE MECHANISM OF THE HEART BEAT.

It is well known that there are two views held as to the cause of the heart beat—*the muscular* or *myogenic* and the *nervous* or *neurogenic*. Our statements of these views must, in the case of mammalian hearts, be more definite than was necessary before the details of the structure and functions of the heart tissue became so well understood.

According to the myogenic theory, the impulse is initiated in the peculiar muscle cells of the *S–A* node unless their irritability is exceeded by that of some other portion of the His-Tawara system (*e. g.*, in the *A–V* node), in which case the muscle cells of this region become the rhythmic center or "pacemaker." The impulse is conducted by the peculiar muscle fibers of the His-Tawara system to the fibers of the auricle and ventricle. The irritability and conductivity of these muscle fibers is under the control of vagus and sympathetic fibers relayed through ganglion cells and their axones.

According to the neurogenic hypothesis, it is necessary to assume that the inner stimulus originates in the ganglion cells in the vicinity of the *S–A* node or in those of the interauricular septum. It is transmitted by axones to the cells of the *S–A* node, of the *A–V* node, the His-Tawara system or the auricular and ventricular muscles themselves. Moreover, it is not impossible to conceive that one system generates the impulses and the other conducts them, or again that

both the nerve and muscle fibers of the His-Tawara system share the property of conduction.

It may be recorded at once that, without question, the majority of physiologists favor the myogenic view of impulse initiation and conduction. We may, therefore, briefly examine the validity of this belief.

When the existence of a muscular connection between the auricles and ventricles was revealed (Kent, His, Jr.) and it was subsequently shown that this represented but a portion of an extensive conducting system of peculiar muscle fibers; when, moreover, a structure in the form of a *S–A* node was demonstrated, which was apparently the homologue of the sinus venosus, and when this was finally shown to be the seat of initial negativity in the heart, it seemed to many conclusive of the muscular origin of the heart beat. With the subsequent discovery that the *S–A* node and the *A–V* node contain or are related to ganglion cells in their immediate proximity and that the entire His-Tawara system contains many bundles of nerve fibers as well as ganglion cells, the absolute guarantee that nerves are not concerned is not afforded by morphological studies alone. It is necessary, therefore, to seek other evidence.

Greatly in favor of the myogenic hypothesis is the fact that the embryonic heart beats before the nervous elements have wandered in from their extracardial position (Pflüger, His, Jr.). The fact that individual cells grown in artificial media (Burrows) pulsate is corroborative. Important as this fact is, it cannot be regarded as conclusive. Its value depends, of course, on the probability that a tissue that once assumes a function in early life retains this function to the end. That this is not necessarily the case has been shown by the fact that in the limulus heart the beat is originally muscular in character, although later the function is undoubtedly transferred to nerve cells (Carlson).

The demonstration that the *S–A* node shows the first evidence of activity combined with the fact that very few ganglion cells are situated here, speaks in favor of a muscular origin of the beat. The only question that can possibly arise is whether with the most careful technic it is possible to so apply the electrodes that they may not be placed on ganglion cells in the vicinity, or provided such placement is possible, whether the initial current does not reach the surface more readily at the more exposed sinus tissue. The careful experiments of Eyster and Meek and Lewis with very sensitive galvanometers and the application of differential electrodes by Garten and his pupils apparently negative such an objection.

The Ultimate Mechanisms.—The so-called fundamental properties of cardiac tissue (rhythmicity, conductivity, irritability and contractility) are, after all, no more than tangible expressions of underlying physiochemical changes taking place within the cells. A correlated study of the chemical, thermal and electrical changes has made it

possible to formulate a probable hypothesis as to the nature of the ultimate mechanisms involved in the heart beat. This is especially true as regards the ultimate events concerned with excitation and contraction (Frank, A. V. Hill, Meyerhoff, Snyder).

The mechanism of the muscle cells may be compared to an accumulator which gradually stores potential energy as a result of some oxidative process, and then swiftly and completely discharges without the involvement of oxidative change. In detail the discharge of energy subsequent to stimulation is apparently concerned with an explosive change of glycogen to glucose and this in turn to lactic acid. This liberated acid, either by changing the surface tension of longitudinal surfaces or membranes or by causing a swelling of colloids, results in a change of length and tension—phenomena associated with the physiological property designated as contraction. Owing to a thermo-elastic effect,[1] heat is liberated in order to neutralize the resulting stress under which the fibers are placed (Snyder). As a result, an accumulation of ions on the surface of the excited area results instantaneously. All of these changes occur without oxidation processes, *i. e.*, is an anaërobic or anoxybiotic process. According to Frey, alteration in amplitude, form and duration of contraction may hypothetically depend on the amount of energy accumulated. Thus, the release of a greater charge may either be accomplished by a more rapid rate of discharge or a more prolonged discharge. Similarly, the transformation of large amounts of glycogen to lactic acid may conceivably result in larger and steeper contractions in prolonged contractions, or both.

What are the physicochemical processes concerned in reaccumulation of energy. Experimental work tends to indicate that oxidative processes are not recognizable until relaxation has been completed, *i. e.*, until the rest phase supervenes. During this interval a part of the lactic acid (one-fifth) is oxidized, the remainder (four-fifths) is reconverted into glycogen (Meyerhoff). The energy of these chemical changes is partly transferred into heat (second or diastolic rise of the thermocardiogram—Snyder), but partly accumulated as the energy which renders the muscle ready again for performing muscular contractions. It remains to interpret the processes taking place during relaxation. If oxidative chemical changes occur they are not indicated by thermal changes, for the temperature markedly decreases during relaxation (Snyder), owing in part at least to endothermic processes concerned when the contractile stress is released. The question as to whether the gradual return of excitability known to occur during the process of relaxation has nothing to do with oxidative processes, and if not, through what ultimate physicochemical changes it is mediated demands attention. Several suggestions have been offered:

[1] For a clear explanation of the thermo-elastic properties of muscle, see Hill, A. V.: Physiol. Reviews, 1922, **2**, 318.

1. The return of excitability may be due to the fact that electrically changed ions slowly diffuse away from active surfaces into the surrounding medium.

2. The lactic acid may combine with some intermediary body, possibly an alkali protein (v. Kries, Hill), which fixes it and thus restores irritability.

3. The tendency to rebuild and burn lactic acid may exist during relaxation, but be inhibited by the concentration of CO_2 driven out of its fixed combinations by lactic acid. As the CO_2 gradually diffuses into surrounding medium, the rate of oxidation speeds up and is the cause of recovery in irritability (Frey).

To summarize, it may be said that muscular contraction may be separated into three phases:

(*a*) Contraction due to the complete and explosive liberation of a form of energy under anaërobic conditions.

(*b*) Relaxation, during which some of this energy is gradually restored either (1) by diffusion of ions from previously active surfaces, (2) by fixation of lactic acid by tissue alkalies, or (3) by progressively increasing oxidation processes as yet unrecognized as temperature variations because of predominant opposite changes.

(*c*) Rest or recovery, during which the energy is fully reaccumulated by oxidative processes.

As regards the fundamental processes concerned in rhythmicity, we may suppose that a similar accumulation of energy connected with glycogen synthesis and lactic acid or carbohydrate oxidation takes place and that the emission of an impulse associated with electrical changes is likewise accompanied by liberation of lactic acid. What, however, sets off the explosive? As in the case of the respiratory center and intestinal tract, an external excitant is probably required; likewise, as in the case of these tissues, it is probably a constant excitant, chemical in nature. Experimental work indicates that at least two of these humoral excitants are necessary to ensure periodic discharges in rhythmic tissue generally, viz., a proper balance of the salts of Na, Ca and K and the presence of at least threshold quantities of CO_2 (Mansfeld and Szent-Györgyi). As to the manner in which salt ions act to cause spontaneous beats in muscle cells, several views are held. Lingle and Loeb believe that sodium ions act as an excitant while calcium antagonizes the poisonous effects of sodium. Howell believes that calcium converts the stable material into an unstable compound in which process potassium is liberated. According to this view, the salts are not direct excitants, but liberate energy of some form which acts in this role. Martin has elaborated the idea further. He thinks that while calcium converts the stable substance into an unstable one, sodium or some other agent is necessary to force this substance to liberate its energy.

Finally, Mines was led to believe that ions are concerned in func-

tional activity because they produce electrical charges on the surface membranes, this being necessary in order that they may possess a differential ionic permeability. He divides ions into three classes: (*a*) "Nomadic ions" (*e. g.*, Na, K, Cl, NO_3), which, as they wander from one region to another, carry electrical charges with them and so set up differences in potential; (*b*) "combining ions" (*e. g.*, Ca); and (*c*) "polarizing ions" (*e. g.*, Mg, OH), capable of changing ionic permeability of surface membranes and thus affecting differentially the passage of nomadic ions.

Closely related to the question of the source of the *inner stimulus* is that relating to the mechanism by which vagus and accelerator nerves modify the heart. For the maintenance of nerve action a proper balance of calcium and potassium is also essential (Howell and Duke, Busquet and Pachon, Hagan and Ormond, Holm and Pick, Cate). The function of calcium in producing inhibition apparently consists in aiding the transmission of vagus impulses rather than in producing an inhibitory effect on the heart muscle. The latter function is attributed to potassium by Howell and Duke, who regard vagus and potassium inhibitions as similar conditions.

The most commonly accepted version of nerve action is that advanced by Gaskell, who regards the vagus nerve as anabolic or trophic and the accelerator nerve as catabolic or motor in character. It may be pointed out that recent work has adduced evidence in favor of his views. In the first place, it has been possible after many failures to corroborate the observations of Gaskell that the auricle in the terrapin becomes increasingly positive with respect to an injured part when the vagus is stimulated (Meek and Eyster, Cruickshank). The failure to obtain this response in mammals is probably accounted for by the fact that it is impossible to use sufficiently sensitive strings in their investigation. In the second place it has been reported that the beat of a stopped heart may be revived by stimulating the accelerator nerves (Hering), while premature systoles have been produced in the beating heart in the same manner (Rothberger and Winterberg).

Still other theories as to vagus action evolved as a result of the investigation of different phases of cardiac activity have been suggested by Carlson, Erlanger and Schmiedeberg, for which the original articles may be consulted (see literature).

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CHAPTER II.

THE SEQUENCE OF CARDIAC CONTRACTION AND THE MOVEMENTS OF THE HEART.

THE CARDIAC CYCLE.

Direct inspection or relatively simple modes of registration are sufficient to establish the general contraction sequence in the different cardiac chambers. Auricular contraction is usually regarded as initiating the cycle of events. During its relaxation and subsequent resting state the ventricles first contract and then relax. These series of events which are repeated in successive beats are designated as the *cardiac cycle.* The term *systole* is generally used to designate the period of muscular contraction in any chamber, while the term *diastole* has come to include both the physiological relaxation process and any possible period of quiescence. We may, therefore, speak of four events—that is to say, *auricular* and *ventricular systoles and diastoles.* As auricular diastole occurs during the combined phases of ventricular systole and diastole, however, it has sometimes seemed advantageous to relate all events to the ventricle and describe only three phases. Thus, the cardiac cycle may be described as consisting of *auricular presystole, ventricular systole* and *ventricular diastole.* It is generally supposed that in the mammalian heart auricular systole terminates before that of the ventricle begins, *i. e.*, that a short *intersystolic interval* exists (Chauveau, Pachon). An examination of such myograms as have been published by various investigators shows that this is apparently true in the majority of cases, but in some records auricular systole either ceases exactly at the beginning or at times continues slightly into the phase of ventricular systole. While these differences are undoubtedly due in part to the variable efficiency of recording mechanisms, there is no doubt that some variation actually occurs in different animals. In restudying this question by optical methods the author has found that this interval varies from 0 to 0.068 second, averaging 0.024 second in the majority of experiments. We may conclude, therefore, that in the great majority of animals a short intersystolic interval actually exists.

The Nature of Auricular Systole.—It has already been indicated that not all portions of the auricles are excited simultaneously, that, on the contrary, the excitation wave spreads from the S–A node to the more outlying portions of the auricular musculature (*cf.* page 31).

It has been estimated that about 0.02 second after each unit of cardiac muscle is excited it begins to contract (Lewis, Feil and Stroud). This contraction of the individual muscle unit has been designated as the *fractionate contraction* (Wiggers) and lasts for a few hundredths of a second (average 0.06, Lewis, Feil and Stroud; 0.047 second, Wiggers). When the approximation of two widely separated points on the auricles is recorded by a myocardiograph of adequate efficiency (Fig. 2) the myogram so obtained gives evidence by its changing gradient that the onset of contraction develops at one point before it does at another. Thus, in the mechanical contraction curves shown in the upper tracings of Fig. 11 it is obvious that the gradient of the downstroke (which indicates rate of shortening) alters in steepness at A^1 and C. The following interpretation of these changes has been suggested by the author:

1. A protosystolic phase lasting about 0.02 second first occurs, during which the rate of contraction gradually accelerates (A–A^1). As interpreted by the diagram inscribed on the curve, this phase probably represents the spread of the fractionate contractions from the proximal to the distal point.
2. A mesosystolic phase (A^1–B), lasting about 0.024 second, follows, during which contraction proceeds at a uniform and maximum rate. This represents the interval during which all muscular tissue is contracting.
3. A telesystolic phase (B–C), lasting approximately 0.03 second, during which the rate of contraction is progressively diminishing, completes the contraction. During this stage the fractionate contractions of the more proximal portions are progressively converted into fractionate relaxations which oppose and tend to neutralize the fractionate contractions of the more distal portions of the tissue. This continues until an exact neutralization at the apex of the mechanical curve has taken place—a point which we term the end of mechanical contraction (C).

These three phases are followed by a phase lasting 0.03 second or less, during which the curve turns upward with a very gradual gradient, owing to the fact that the fractional relaxations are beginning to predominate over the fractional contractions (C–D).

If these interpretations prove correct then the apex of the mechanical contraction does not indicate the moment when all the fractionate contractions have ceased. At B, some of the fractions of cardiac tissue have started to relax and, to a distance beyond C, other fractions still continue to contract.

A comparison of simultaneous auricular pressure curves with such myograms (Fig. 11) further shows that the initial contraction of fractions lying still nearer to the S–A node are not incorporated in myograms taken from the anterior auricular surface. It is quite obvious, therefore, that a myogram thus recorded shows neither the

onset of the first fractionate contractions, nor does it indicate when the last fractions cease to contract. We are, therefore, confronted

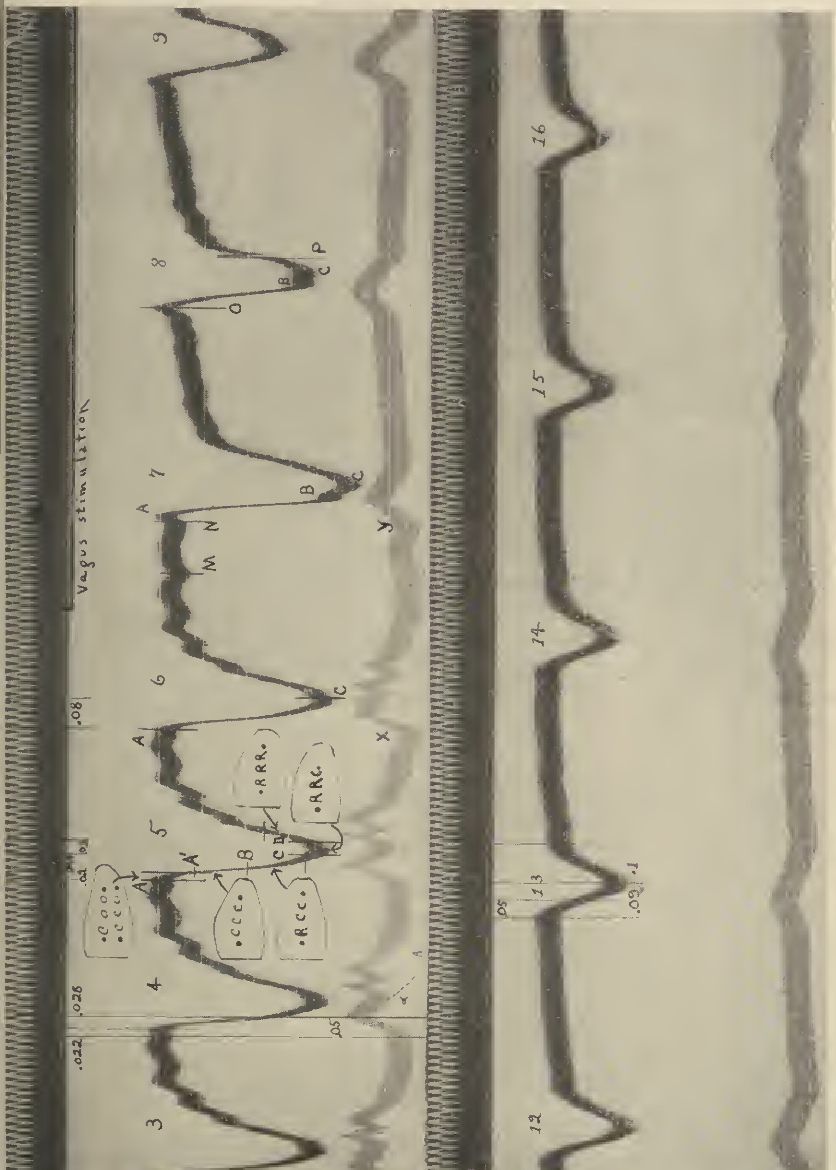

FIG. 11.—Auricular myogram (upper) and intra-auricular pressure curve (lower) illustrating the nature of auricular contraction; *X–A*, interval of auricular contraction (.022 sec.) before anterior surface of right auricle is affected; *A–A*[1], period of progressive spread of contraction; *A*[1]*–B*, summation of fractionate contractions between myocardiograph attachments; *B–C*, relaxation of fractions near proximal attachment but with contracting units predominating; *C*, balance of contracting and relaxing units; *D*, end of all fractionate contractions. *X–C*, auricular systole; lines cutting pressure curve in beat No. 4, dynamic interval of systole. Effect of left vagus stimulation demonstrates (1) the larger beat immediately following stimulation when rate changes occur during stimulation (2) removal of accidental vibrations from auricular myograms when ventricle does not beat (3) depression of contractility and (4) influence of left vagus nerve on *S–A* as well as *A–V* bundle.

with the necessity of selecting more precise criteria for determining the interval of auricular systole.

In conformity with the generally accepted definition of auricular systole, viz., that it represents *the period during which the entire auricular musculature is mechanically shortened,* the author has suggested that systole be estimated as the time interval between the beginning of the rise of intra-auricular pressure and the end of the mechanical contraction established by the myocardiogram, *i. e.,* in Fig. 11 from X to C (fourth beat).

Curves such as are shown in Fig. 11 make it obvious at once that the intra-auricular pressure curve is of even less value in determining the duration of systole than is the auricular myogram. Auricular systole continues to develop tension, as indicated by the rise of the intra-auricular pressure curve, only as long as all muscular units continue to contract. As soon as evidence appears in the myogram that the curve is a resultant of fractionate contraction and relaxation processes, the intra-auricular pressure curve falls. The period during which tension is developed lasts about 0.053 second and may be designated as the *dynamic period of auricular systole.* As there is a delay in the excitation of the more distal portions of the right auricle, so also the excitation of the left auricle is still more delayed. This has the effect that both systole and diastole begin about 0.013 second later in the left auricle (Chauveau, Bachmann, Wiggers and Katz)—in other words, an *interauricular contraction interval* exists.

The Nature of Ventricular Systole.—Considerable discussion has centered upon the question as to whether or not all portions of the ventricular musculature also begin and end their contractions simultaneously. In deciding this question ventricular myograms are of no value—recorded by levers on smoked surfaces they are inexact, recorded by adequate optical systems they are rendered unintelligible, owing to the fact that the heart sounds are also picked up.

The spread of the excitation wave indicates, however, that the papillary muscles and the endocardial surfaces are excited before the epicardial surfaces, and of the latter the right appears to be excited slightly in advance of the left (*cf.* page 33). Assuming the latent period of all ventricular muscle to be equal, we may suppose: (1) That the papillary muscles contract slightly in advance of the rest of the heart and (2) that the right heart contracts slightly in advance of the left. The first supposition is supported by direct experiments, which indicate that the contraction of the papillary muscles precedes the contraction of the conus arteriosus by 0.015 to 0.031 second (Hering, Saltzman). The second supposition is not, however, borne out by studies of intraventricular pressure curves from the right and left ventricle, which, under normal conditions, show a simultaneous increase in pressures on the two sides (*cf.* Fig. 168). Unless work to the contrary is adduced, it is, therefore, necessary to assume that both ventricles begin and end their contractions simultaneously. Whether all fractions partake of the inception of ventricular systole and whether

certain fibers continue to contract after the majority have relaxed somewhat, as in the case of the auricles, cannot now be answered with certainty. This question is, however, of academic rather than practical importance, as systole must be considered as ending when the expulsion of blood ceases.

As the ventricles are concerned primarily with the work of ejecting blood against an arterial pressure, the physiological nature of ventricular contraction can be compared to that of a skeletal muscle performing work. The ventricular muscle does not alter its length during the entire period of systole, but, in its early phases, operates as an after-loaded muscle. Henderson has pointed out that the heart, with certain minor reservations, operates as a skeletal muscle attached to a work adder. In such an arrangement (Fig. 12) the weight (W_1)

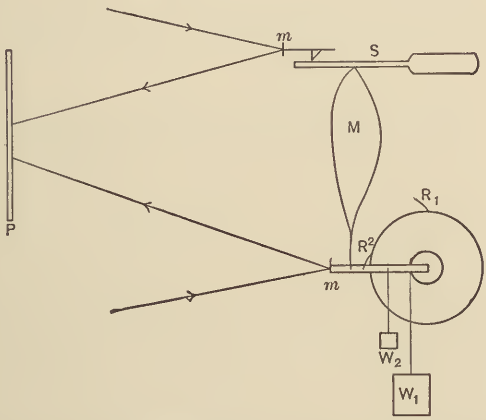

FIG. 12.—Diagram showing arrangement of muscle activitating a work adder. S, stiff spring; *m*, small mirrors reflecting light beams to photographic film, P. Further description in text.

which the muscle is required to lift is supported by the ratchet R_1, and, consequently, weights the muscle only during contraction. During the rest period, as well as during the process of relaxation, the muscle is stretched by a smaller weight, W_2. Obviously, the greater this weight becomes the greater the length of the resting muscle. This resting length of the muscle is referred to as its *initial length*. When this weight increases the muscle fibers are not only lengthened, but are also placed under a greater tension, referred to as the *initial tension*. Changes in this initial tension may be recorded graphically and evaluated by attaching the upper end of the muscle to a stiff spring, the very slight movements of which can be greatly magnified and projected (Fig. 12). A muscle so arranged is said to be "after-loaded." Before it can shorten, its tension must be increased sufficiently to overcome the load W_1, *i. e.*, it first contracts *isometrically*.

Such a tension variation will be recorded by the upper lever a short interval before the lower lever begins to register a decrease in length. This accomplished, the ratchet R_2 engages and the weight is raised during the remainder of the contraction phase. Inasmuch as the tension during this phase of contraction does not alter appreciably, it is said to contract in an isotonic manner. At the onset of relaxation the ratchet lever R_1 engages and the relaxation process is assisted by the small weight W_2.

In the normally beating heart the venous pressure represents the distending load W_2 and determines the initial tension as well as the initial length of the ventricular muscle fibers, while the arterial pressure corresponds to the lifted load W_1. The engagement of ratchet R_2 corresponds to the closure of the *A–V* valves and its disengagement at the end of contraction to their opening; similarly the disengagement of rachet R_1 corresponds to the opening of the semilunar valves and its reëngagement at the end of contraction to their closure.

THE MOVEMENTS OF THE HEART.

During ventricular systole all diameters of the heart decrease and the position of the entire organ changes. These changes are due in part to the spiral arrangement of muscle bands in the ventricles, in part, also, to its fixation and support. The anatomical researches of MacCallum and their subsequent extension by Mall have shown that the two ventricles are made up of a series of muscular bands passing from the base to the apex in the form of a scroll. Mall divides these fibers into four groups, viz.: (1) The superficial bulbo-spiral fibers, (2) the superficial sino-spiral fibers, (3) the deep bulbo-spiral fibers and (4) the deep sino-spiral fibers.

The superficial bulbo-spiral fibers arise from the conus arteriosus and the left side of the aorta and auriculo-ventricular ring and pass down obliquely to the apex, where they form a spiral and thus reach the interior of the ventricle to terminate in the interventricular septum and posterior papillary muscle. The superficial sino-spiral fibers arise from the posterior portion of the *A–V* ring, run obliquely to and over the anterior surface of the right ventricle, and, after reaching the apex, pass by a spiral turn inward to end in the anterior papillary muscles of the left heart. The deep bulbo-spiral fibers are attached to the dorsal side of the aorta and encircle the left ventricle. The deep sino-spiral fibers encircle the right ventricle in similar fashion.

When the heart is exposed in the open chest and the pericardium is removed, or when it is suspended from the large vessels in perfusion experiments, the effect of these muscular bands is brought into play. The base remains practically stationary or moves upward slightly, but the apex moves upward to a marked extent. The entire heart is

caused to rotate from left to right by the oblique fibers and the apex is lifted forward.

If, however, the movements of the heart are studied when only the upper three-fourths of the sternum is resected, so that pericardial attachments remain intact, and if, in addition, the severed sterno-cardial bands are fastened to a wire substituted for the sternum the base descends, the apex rotates anteriorly and in so doing moves downward slightly during the early phase of systole, then is slightly pulled upward again. If the animal is placed on the left side so that the heart is definitely in contact with the thoracic wall, it is evident that the slight downward movement of the apex is largely responsible for the impact felt externally as the apex beat. (Personal observations.) These differences between the movements of the free and the intact heart are due to the restraining influence which the pericardium exerts. This covering is attached to the large vessels at the base of the heart, stretches upward into the cervical fascia and joins the central tendon of the diaphragm below. As blood is ejected and the ventricular muscle shortens, the diaphragmatic attachment of the inelastic pericardium prevents the natural upward movements of the base and consequently, assisted by the elastic recoil of the heart and the tendency to develop a negative pressure within the pericardium, the base approaches the apex.

It appears from roentgen-ray studies (Dietlen, Eyster and Meek) that the movements in man are similar to those directly observed in the dog's chest by special technic. These observations favor the view that the slight downward movement of the apex and its slight rotation and consequently its closer apposition to the chest wall account for the major part of the shock felt in the fifth intercostal space. It seems very questionable, indeed, whether changes in the volume of the heart or variations of intraventricular pressure are in the least concerned in the production of the cardiogram obtained by graphically recording the apex beat.

The heart shifts its position not only in systole and diastole, but also during phases of respiration, a change accounted for by the intimate relation of the heart and diaphragm.

Fluoroscopic examination, instantaneous roentgen-ray exposures, orthodiagrams, as well as the roentgen cinematograph, have combined to show that the entire heart moves downward and that the apex is rotated clockwise during inspiration. The shadow of the entire heart lengthens and becomes narrower (Fig. 13). Corroborative evidence that the cardiac axis changes have also been given by the electrocardiograph (Waller, Einthoven), it having been shown by computation of the electrocardiac angle from the height of ventricular waves that expiration causes the heart to become more horizontal (*cf.* page 287).

There is further evidence in dogs that the apex descends in

inspiration. The writer has frequently found that when a sound is accidentally placed deep in the ventricular chamber the end is open throughout systole only during those beats occurring in inspiration, while during expiration either no pressure changes are recorded or a flat-top type of curve due to blocking of a sound by ventricular contraction is obtained.

The exact mechanism by which the position of the heart is changed in inspiration has been studied by attaching strings to five or six different points of the heart intact within the pericardium and connecting these simultaneously to recording levers (Wiggers). The following observations were made:

1. During the descent of the diaphragm the posterior portions of the heart and the venæ cavæ descend more than the anterior portion of the base, while the anterior aspects of the apex move forward and as a result often slightly upward. The right and left borders of the ventricle move toward the right.

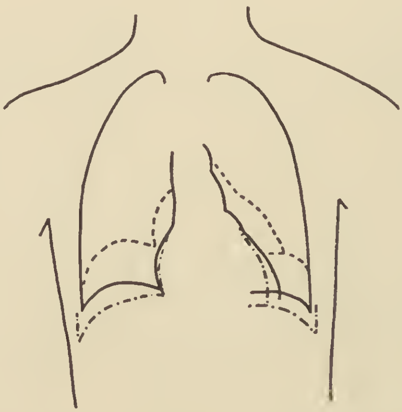

Fig. 13.—Orthodiagram showing the effect of deep inspiration and expiration on the positions of the heart and diaphragm. Broken lines, expiration; dots and dashes, deep inspiration; continuous line, shallow respiration. (After Claytor and Merrill.)

2. The movement of the heart to the right does not occur after severing the left phrenic nerves nor upon stimulating the right phrenic nerve. It is, therefore, due to a traction of the left sheath of the pericardium.

3. A descent of the base of the ventricles, the auricles and the venæ cavæ occurs after the entire pericardium is severed from the diaphragm. Direct experiments show that this is due in part to a traction upon the inferior vena cava, making it longer and narrower.

4. In the dog the descent of the base of the heart persists after the vena cava is clamped and divided. This results from a traction upon the ligamentum pulmonale (a double fold continuous with the pleura

pulmonalis and passing downward from the root of the lung to its vertebral and diaphragmatic attachments) which causes the roots of the lungs, the pulmonary vessels and, through these, the base of the heart to move downward.

Studies with the roentgen rays and electrocardiograph indicate that the position of the heart is not as fixed as has often been supposed, but that, on the contrary, it undergoes considerable shifting with the position of the diaphragm and changes in different positions of the body. The heart is displaced to the left when the left lateral position is assumed and the apex approximates the chest wall more firmly, a point of some significance in recording tracings from the apex region. A change from the supine to the prone position causes a compression of the abdominal viscera and so pushes the diaphragm up, which causes the heart to assume a more horizontal angle. Sitting acts in a similar way, but to a lesser degree, by compressing the abdominal contents.

In addition to modifying the movements of the heart and altering its position during its respiratory phases, the pericardium has a protective function in checking excessive filling. This enclosing sac is not only exceedingly inelastic, but capable of withstanding very considerable pressures (Barnard). Kuno has found that, in the absence of this protective covering, it is difficult to increase the work of the heart above normal limits without the supervention of myocardial insufficiency.

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Pachon: Arch. physiol. et path. gén., 1909, **11**, 377 (*intersystolic interval, literature*).

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For literature dealing with the roentgen ray and electrocardiographic investigation of cardiac position, consult references at the end of their respective chapters.

CHAPTER III.

THE DYNAMICS OF THE HEART BEAT.

THE "dynamics of the heart beat" is concerned with the mechanisms by which the heart transfers the blood from the venous to the arterial side under sufficient pressure to ensure its circulation around the body. It involves a study of (1) the mechanism of the valve action, (2) the pressure relations obtaining at different times in the different chambers and (3) the passage of blood to and from the ventricles.

THE MECHANISM OF VALVE ACTION.

The atrio-ventricular and aortic orifices of the two ventricles are guarded by exceedingly efficient sets of valves.

A *B* *C*

FIG. 14.—Three diagrams showing mechanisms concerned in valve closure. *A*, relations of papillary muscles and chordæ tendineæ to valve flaps; *B*, partial closure due to eddy formation; *C*, closure by hinge movement and breaking of a jet.

The mitral and tricuspid valves arise from the atrio-ventricular ring. They are divided by deep incisions into two flaps on the left side and into three flaps on the right. At their origin the valves are fairly thick and contain strands of muscle tissue (Kürchner, Kent), which have been observed to have a contractile function (Erlanger), but toward their free edges they become exceedingly thin. In fact, such thin structures can resist pressure only because they approximate in a lateral fashion. Into the free ventricular surfaces of the valves are inserted the chordæ tendineæ arising from the papillary muscles which project into the ventricles (Fig. 14, *A*). Their function is apparently to prevent or guard against a possible inversion of the valves into the

auricles. During diastole these tendons are somewhat relaxed, but as the valves close they are rendered taut. This is assisted by the contraction and shortening of the papillary muscles.

It is generally regarded as established (Baumgarten) that the valves in diastole do not lie in close proximity to the heart wall, but float together as blood rushes in. This is, no doubt, partly accounted for by their extreme lightness, but is aided also by the formation of eddies behind them during the inrush of blood which takes place in diastole.

The semilunar valves guarding the pulmonary artery and aorta consist essentially of three small pockets, the free edges of which, when the pockets are expanded, form a complete closure of the aortic opening. Their shape and the support offered by their attachment are such that no sustaining chordæ are required. Exactly at the center of the rim of each pocket is a tiny nodule, the corpus Arantii. These together fill the small central gap that would otherwise be left when the pockets expand. Like the semilunar valves, they are floated away from the wall even during systole, owing to the fact that some fluid remains within them constantly and that eddies are formed behind them.

Three groups of opinions have been held as to the factors responsible for closure of the *A–V* valves, viz.: (1) That closure is due to active muscular contraction; (2) that it occurs passively; and (3) that it occurs by both processes. (For literature *cf.* Lian, R. Tigerstedt). Active closure has been referred to a contraction of the papillary muscles, to a narrowing of the *A–V* orifice by muscular contraction and to a contraction of the intravalvular muscle fibers lifting the valves into position. While it cannot be denied that these factors may be concerned in efficient valve closure, it is now generally regarded as demonstrated that closure is chiefly the result of passive dynamic influences. Most investigators have adhered to the classical views advanced by Chauveau and Faivre, viz., that the valves are still open at the end of auricular systole and closed by the elevation of intraventricular pressure during ventricular systole. Other observers, however (Baumgarten, Henderson and Johnson), believe that the valves are firmly closed before the onset of ventricular contraction and that contraction of the auricle is really responsible for their closure. The physical mechanisms have been most clearly stated by Henderson and Johnson. According to these investigators, the sudden cessation of flow from auricle to ventricle causes the "breaking of a jet," which leaves an area of negative pressure "much as in the wake of a ship." From each side fluid is drawn in and with it the valves are unrolled and closed.

The chief evidence which cannot be harmonized with such a view may be briefly summarized as follows:

(*a*) Inspection of neither the auricular pressure nor the ventricular volume curves supports the necessary assumption that auricular injec-

tion *stops abruptly;* on the contrary, the gradually rounded summits indicate a gradual cessation of inflow.

(*b*) As closure of the *A–V* valves is accompanied by a sound, we should expect presystolic sound vibrations if valvular closure were a presystolic event. Not only is this not the case, but the recorded first sound increases abruptly in intensity shortly after the increase of intraventricular tension (*cf.* Fig. 107).

(*c*) Intra-auricular pressures increase slightly during the early phase of ventricular contraction, which may be explained as due to a closure of the *A–V* valves (*cf.* Fig. 110).

(*d*) Direct records of the mitral valve movements in a perfused heart show that while the valves float toward a position of closure during auricular systole, complete closure accompanied by sound vibrations never occurs unless a subsequent ventricular systole follows (Dean) (Fig. 15).

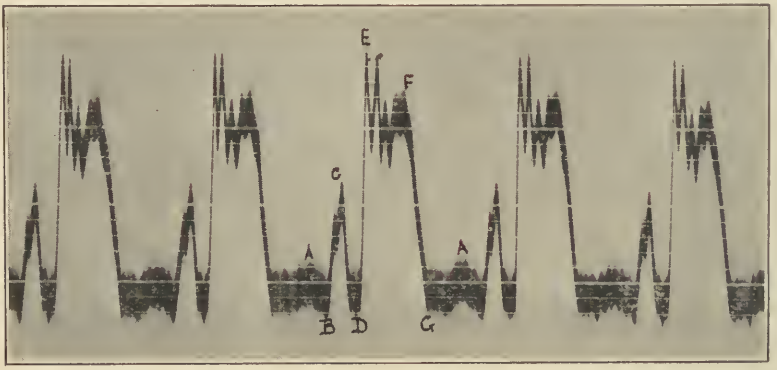

FIG. 15.—Optical records of movements of mitral valve when normal sequence and a long *As–Vs* interval obtain. *B C*, auricular closure of valves; *D E*, ventricular closure; *E F*, sound vibrations after complete closure. (After Dean, Jr.)

The detailed mechanism by means of which the valves are closed without regurgitation can be variously interpreted. Following the conception advanced by Krehl, it is generally held that closure is brought about by the eddies set up behind the valves when fluid rapidly passes through their openings. When the flow ceases the eddy circles enlarge, much as a spring or coil, thus floating the valves together as soon as the pressure on the concave side during ventricular systole becomes a trifle higher than on the auricular side (Fig. 14, *B*). Henderson and Johnson have reported experiments which indicate that, under such conditions, the valves close by a hinge movement, *i. e.*, swing like a door from the point of their insertion (Fig. 14, *C*, 1–2). They stress the fact that this necessarily involves a slight regurgitation. When, on the contrary, the valves close as a result of the breaking of the jet they tend to unroll much as a rug over an opening in

the floor. Such a mode of closure is not accompanied by regurgitation. They believe that the *A–V* valves close in this way when blood is rushing in during auricular systole and when the heart rate is rapid. When, however, the heart rate is slow so that filling has been completed before the beginning of systole, or when the auricles are not beating, the valves do not unfurl but swing into place like doors on hinges (Fig. 14, *C*).

The relative importance of auricular systole and increase of intraventricular pressure in valve closure has been directly investigated by Dean by attaching a delicate hair to the septal flap of the mitral valves and transmitting its movements to a delicate optical system. This investigator arrived at the following conclusions:

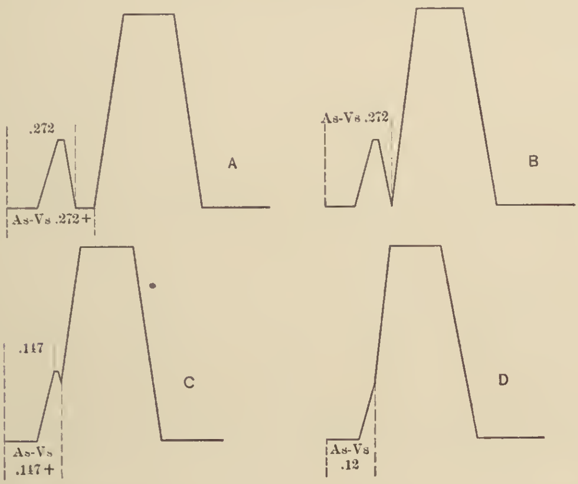

Fig. 16.—Schematic drawing showing influence of length of *As–Vs* interval on valve movements. (After Dean, Jr.)

A short interval after the onset of auricular systole the mitral flaps move toward the ventricle slightly (Fig. 15, *A–B*), then float toward a position of closure (*B–C*) and after that to their previous position (*C–D*). With the onset of ventricular contraction at *D* the valves close quickly and show sound vibrations (*E–F*). At the end of systole (*F–G*) they rapidly open. It is clear that while auricular systole floats the valves *toward* a position of closure, they open again and are closed again effectively by ventricular systole. Such events occur only when the *As–Vs* interval is unusually long (0.272 second). As this interval decreases to 0.147 second, time for a complete opening of the valves is lacking before ventricular systole completes their closure. When this interval becomes less than 0.147 second, as is normally the case, the *A–V* valves have no time to open and are consequently in the process of closure when ventricular systole begins. *Ventricular*

systole thus completes the closure already initiated by auricular systole. This conception, it may be noted, has recently been accepted by Henderson as normal for the heart. The effects of variation in the *As–Vs* interval are clearly shown in Fig. 16.

THE PRESSURE CHANGES IN THE HEART AND BLOODVESSELS.

Apparatus.—The variations of pressure in the chambers of the heart and aorta occur so rapidly that, as has long been recognized, the mercury manometer is incapable of following the changes accurately. This is due to the inertia of the mercury, *i. e.*, the physical property by virtue of which it resists being set in motion when at rest and strives to remain in motion after the acting force has ceased. This causes the apparatus to record an amplitude which does not correspond to the pressure changes actually involved. If a high pressure is suddenly communicated to a manometer and then released the mercury rises above and falls below the true level. The amplitude of the curves is larger than the true variation. If the variations recur rapidly, however, neither the highest nor the lowest pressures are approached and the recorded amplitude is less than the change which actually occurs. This is the case when the mercury manometer registers pressures within the heart and large vessels. Not only are the extremes of pressure incorrectly recorded, but the rise starts later and lags behind the pressure change. In other words, the inertia is determined by the low vibration frequency inherent in the instrument. We return, therefore, to the physical fact that an apparatus, in order to record the oscillations correctly, must have an inherent frequency that is more rapid than that of the most frequent oscillations to be recorded.

Recognizing the limitations of the mercury manometer, attempts have been made by physiologists to devise *membrane* or *spring manometers* capable of correctly following the details and height of the pressure curves. In this they have been relatively unsuccessful, however, until Frank worked out the mathematical and theoretical basis for the construction of adequate types. Frank's critique constitutes, therefore, the most important contribution yet made to the study of the dynamics of the circulation.

Theory of Manometers.—According to Frank the "*manometer*" *constitutes the entire pressure-recording system extending from the rubber capsule and recording point to the mouth of the cannula in the artery.* The efficiency of any instrument (Güte) is expressed by the formula $G = \frac{v\,\gamma e\,E'}{M'}$ where v is the magnification of the lever, γe the sensitiveness of the membrane, E' is the volume-elasticity coefficient and M' is the effective mass. *By increasing the first three and decreasing the*

last factor, the efficiency of an instrument may be improved. The effective mass M' is dependent directly on the length and the specific gravity of the fluid column and is inversely related to the cross-section, *i. e.*, $M' = \frac{l}{Q}s$, in which l equals the length, Q the cross-section, and s the specific gravity. It is apparent that the *efficiency of the apparatus is augmented whenever the length of the manometer decreases and the width of the tube increases. The sensitiveness* is the ratio of membrane excursion to pressure change, *i. e.*, $\gamma e = \frac{f}{p}$. *The excursion f for a definite pressure change and hence the sensitiveness of the instrument may be increased either by decreasing the tension of the membrane, increasing its diameter or by decreasing the diameter of the supported plate.* This is indicated in the formula $f = \frac{p}{s} \cdot \frac{r^2—q^2}{4}$, in which p is the pressure; s, the tension of the rubber; r, the radius of the rubber, and q, the radius of the plate. The volume-elasticity coefficient E' represented by the ratio of the pressure change to the volume change, on the other hand, may be *increased by increasing the tension or by decreasing the size.* This is shown in the formula $E' = \frac{\triangle p}{\triangle v} = \frac{8s}{r^4(1 - d^4)\pi}$. In this formula $\triangle p$ = pressure increase, $\triangle v$ = volume increase, s = the tension and r = the radius of the membrane. *It is apparent that the increase in efficiency which can be gained by increasing the sensitiveness of the membrane is limited, for in so doing the volume-elasticity coefficient is simultaneously reduced.* Furthermore, the sensitiveness of the membrane must remain small in order that an adequate vibration period may be retained, for upon this depends the ability to record pressure changes accurately.

The inherent vibration frequency, N, is the reciprocal of the period of a single vibration, or, $N = 1/T$. In a simple manometer system $T = 2\pi\sqrt{\frac{M'}{E'}}$. From this it is apparent that the *quality is increased, not only by reducing the effective mass, but also by increasing the volume-elasticity coefficient.* Both are usually necessary to obtain an instrument capable of recording pressure variations.

It is apparent that every increase in quality resulting from a higher volume-elasticity coefficient occurs at the expense of its sensitiveness, hence it becomes necessary to magnify these movements. When this can be brought about by a beam of light the efficiency of the apparatus is improved, for, in this way, v is increased without reducing the quality. When, however, the movements of the membrane are magnified by ponderable levers there must be taken into consideration: (1) The reduced mass of the lever (m) (*i. e.*, the mass which applied at the spot where the force is exerted would have the same effect on the

system as the lever) and (2) the linear elasticity coefficient η (*i. e.*, the distorting effect of pressure on the membrane). In other words, T becomes $2\pi\sqrt{\frac{M'}{E'} + \frac{m}{\eta}}$. The reduced mass of the lever may be calculated by the formula $m = \frac{v^2 L\mu}{3}$. Here v is the magnification, L is the length and μ, the specific mass. It follows that the vibration period becomes longer and the frequency per second less when the length or the specific mass of the lever increases with the magnification.

The application of Frank's guiding principles has enabled several investigators to construct manometers of high vibration frequency to meet the demands of special problems. Frank, himself, constructed the first apparatus for estimating arterial pressure and other forms for studying pressures in the heart have been added by Straub, Piper and Wiggers.

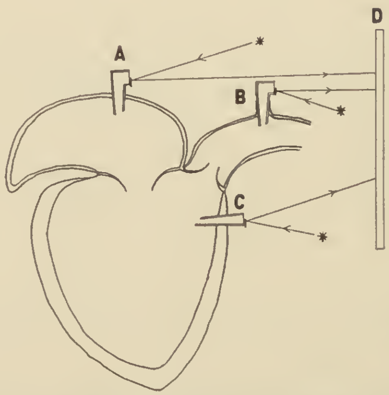

Fig. 17.—Schematic representation of principles employed to record pressure curves optically from the auricles, A, ventricles, C, and aorta, B. D, sensitive photographic surface. Description in text.

Principles of Optical Registration.—The principles employed in the construction, insertion and operation of optical manometers is illustrated in Fig. 17. Suppose that small chambers, A, B and C, filled with fluid and covered by very tensely drawn rubber membranes, are inserted through the auricular and ventricular walls or into the aorta. Each membrane will then respond to every pressure variation by a microscopical movement. This can be magnified and rendered visible by reflecting a narrow band of light from a small mirror fastened to the rubber. By allowing these beams to focus on a film (D) moving in a specially constructed camera, a true picture of the pressure variations can be recorded.

For a number of technical reasons the use of such simple forms of manometers is limited for recording pressure variations in the circu-

lation, chief among which is the fact that it is not sufficiently sensitive, *i. e.*, inscribes records which are of too small amplitude. As a beam of light longer than 150 cm. is not feasible for optical reasons, a greater sensitiveness must be acquired either: (1) By some device which causes the mirror to move more than the membranes or (2) by enlarging the surface of the membrane. The decrease in efficiency involved in either of these methods is not so great but that the instruments are still adequate for studying pressure changes in the cardiac vascular system.

Frank's Arterial Manometer.—In order to record pressure changes from an elastic membrane at some distance from the source of pressure and yet retain the essentials of an ideal manometer, Frank constructed the apparatus shown in Fig. 18. The body of the instrument consists of two vertical glass tubes, *b* and *E*, communicating by a bent horizontal tube, *d*. The vertical tube, *b*, is prolonged downward into a metal cone, *K*, over which the cone of the arterial cannula, *C*, is rigidly attached by the screws, *S*. The vertical projection, *E*, terminates in a small end with a manometer capsule 3 mm. in diameter. The apparatus is filled to the exclusion of the smallest air-bubble by allowing fluid to enter slowly by stop-cock, *f*, the air being allowed to escape at *c*. When completely filled a rubber dam is tensely stretched and tied over the opening at *g* and a tiny glass circlet cemented to it. The very slight excursions of this tense and small membrane are communicated to a tiny mirror (*M*) by a small well-balanced lever, *h*, pivoting on free axes. As the membrane rises, the mirror tilts and causes the slight diaphragm movement to be magnified by reflecting a band of light from an optical lamp (*cf.* page 181). While this instrument was originally designed to record arterial pressure, it has also been employed (C. Tigerstedt) to record intraventricular pressures.

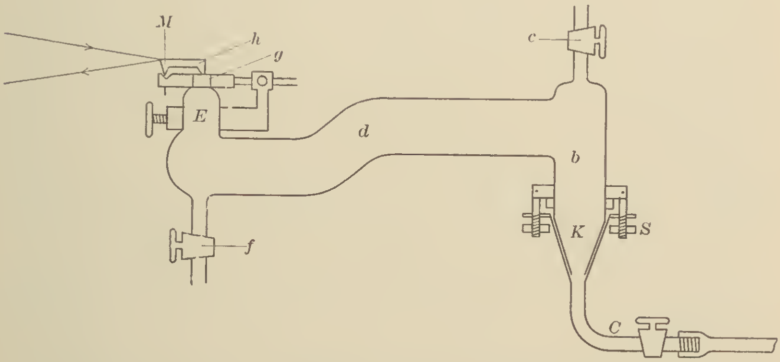

Fig. 18.—Diagram of Frank's manometer.

Manometers for Recording Pressures in the Heart.—Several forms of intraventricular pressure manometers have been devised. The trocar manometers devised by Straub and Piper have the disadvantage that, as the plunger is withdrawn, the apparatus fills with blood which is liable to coagulate and change the damping. A *universal manometer* devised by the author can be employed to record pressures, not only from the cardiac cavities, but from any portion of the arterial or venous system as well. It consists (Fig. 19) of a vertical glass tube, *d*, surmounted by a brass cylinder, *e*, ending in a segment capsule, *b*, 3 mm. in diameter and covered with rubber dam. Upon this a small piece of celluloid carrying a little mirror, *c*, is fastened so that it pivots on the chord side of the segment capsule. Above the recording mirror is mounted a reflecting mirror, *f*, adjustable about a horizontal axis by a screw. The reflection of the light band to a horizontal plane occurs, as shown in Fig. 19. The lower end is fitted by a conical joint with several styles of cannulæ adapted for recording arterial, auricular and ventricular pressures respectively.[1]

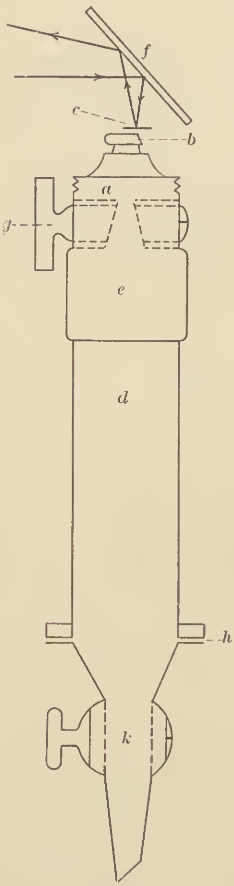

Fig. 19.—Optical manometer for recording intracardiac pressures. (Author's model.)

To record ventricular pressures, the short, straight cannula with a slightly conical shape, as shown in the diagram, is inserted directly through the heart walls in a place where the movement is slight. The entire manometer is then rigidly clamped. To record auricular pressure a short curved cannula is slipped through the ear of the auricle *via* one of the veins and tied.

Contour of Pressure Curves.—The normal pressure curves in the auricles, ventricles, aorta and its branches have been studied by Frank, Straub, Piper, C. Tigerstedt, Garten and the author by means of optical manometers. Although minor differences occur, it is desirable to limit the description to the records that may be regarded as typical, under normal conditions,[2] of the circulation.

[1] The damping plate (*a*) and the stop-cock (*g*) shown in the illustration have been found unnecessary and are, therefore, now omitted.

[2] In this connection, the author regards conditions as "normal" in experimental animals when the form of the arterial pressure curve corresponds to that obtained from the subclavian artery of man by optical methods.

The Intraventricular Pressure Curves (Garten, Piper, Straub, C. Tigerstedt, Wiggers).—The essential features of left intraventricular pressure changes are shown in Fig. 20. The curve is sometimes inaugurated by a small elevation (1–2), due to auricular contraction. This is followed by the large ventricular wave which, by changes in gradient, may be divided into several portions, viz., 2–3, a steep elevation of pressure; 3–4, a gradual increase to its rounded summit (or *pressure maximum*); 4–5, a slow decline; 5–*f*, a sharp incisive drop, and finally a more gradual fall to 6.

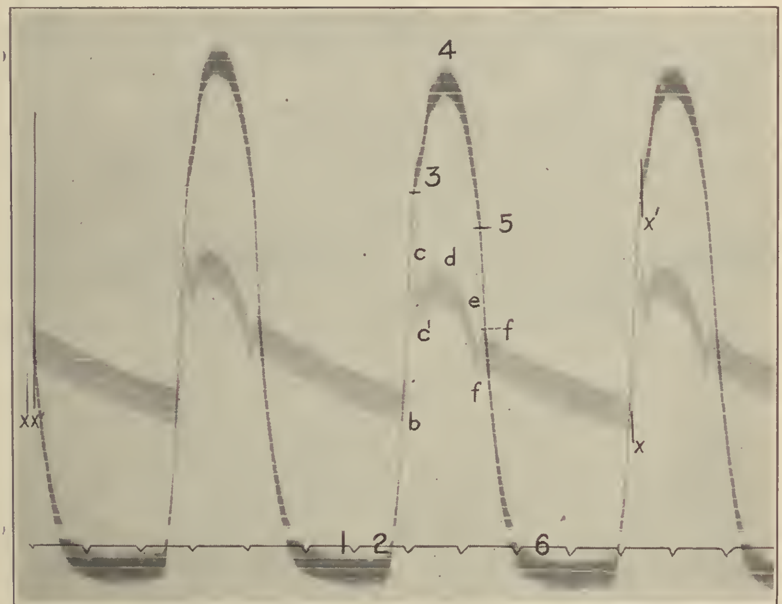

Fig. 20.—Simultaneous intraventricular and subclavian pressure curves. *x–x'*, relative positions; *T*, time in $\frac{1}{5}$ second; 1–2, auricular rise; 2–3, isometric period; 3, opening of semilunar valves; 3–4, ascending limb of ejection period; 4–5, descending limb of ejection phase; 5–*f*, incisura; *f*–6, isometric relaxation; *b–c*, primary oscillation; *d*, systolic summit; *e–f*, incisura.

Considerable discussion has arisen among physiologists as to whether the summit is rounded, as appears in Fig. 20, or whether an ascending or descending plateau, such as shown in Fig. 21, occurs. Both types of curves are found in animals in the case of the left ventricle. These variations, as the author has pointed out, are partly apparent and partly real. The apparent differences depend largely upon the sensitiveness of the manometer used and the speed of the paper on which tracings are taken. Curves of smaller amplitude show much less apparent rounding than those of larger amplitude, and the latter, in turn, appear much more peaked when taken on slow paper, as in Fig. 20.

When such curves are spread out on more rapid paper they also show a gradually ascending but rounded summit, reaching its maximum beyond the middle of the pressure curve, but declining during approximately the latter third. In spite of opinions to the effect that a definite plateau is a normal phenomenon (C. Tigerstedt, Garten, etc.), the writer is inclined to regard these as consequences of abnormal arterial and venous pressures and considers curves, such as illus-

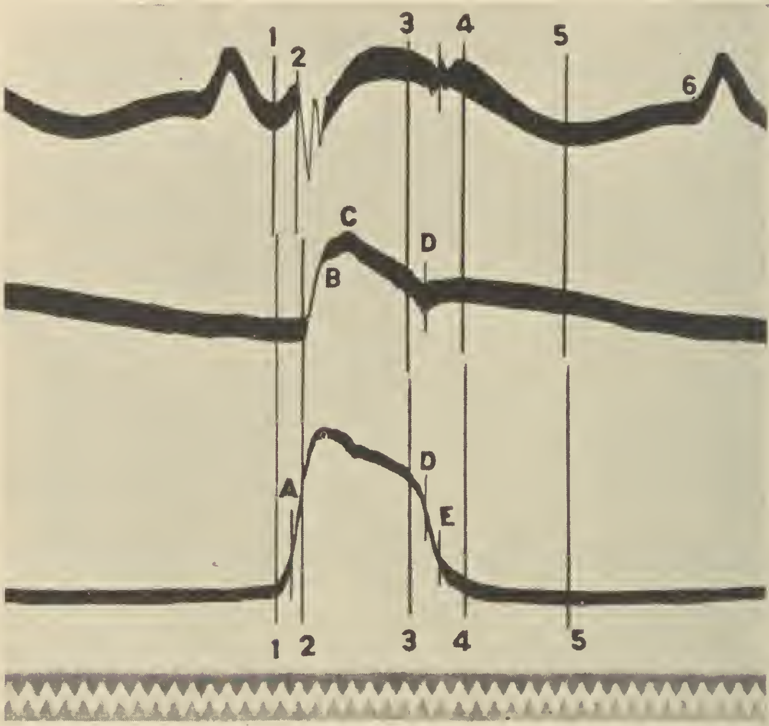

FIG. 21.—Synchronous records of intra-auricular pressure (upper); pulmonary arterial (middle); right ventricular pressure (lower). Tuning fork, 0.02 second; 1–2, isometric contraction phase; 2–3, phases of maximum and reduced ejection; 3–*D*, protodiastolic phase; *D*–4, isometric relaxation phase; 4–5, rapid inflow phase; 5–6, diastasis. Further description in text.

trated in Fig. 20, as normal for the left ventricle of the dog and probably also for man. The author further supports the contention of Frank that a plateau in the sense of unvarying pressure is unthinkable; the pressures must always either rise or fall.

In the right ventricle the curves are essentially different in that the summit may present a more slowly declining plateau, *i. e.*, the summit being reached early. The amplitude of the curve is, of course, less (Fig. 21).

The Arterial Pressure Curves.—The contour of the pressure curves in the central arteries has generally been considered as established by pressure curves taken from the subclavian or innominate arteries (Frank). The chief pressure variations occur during the ejection

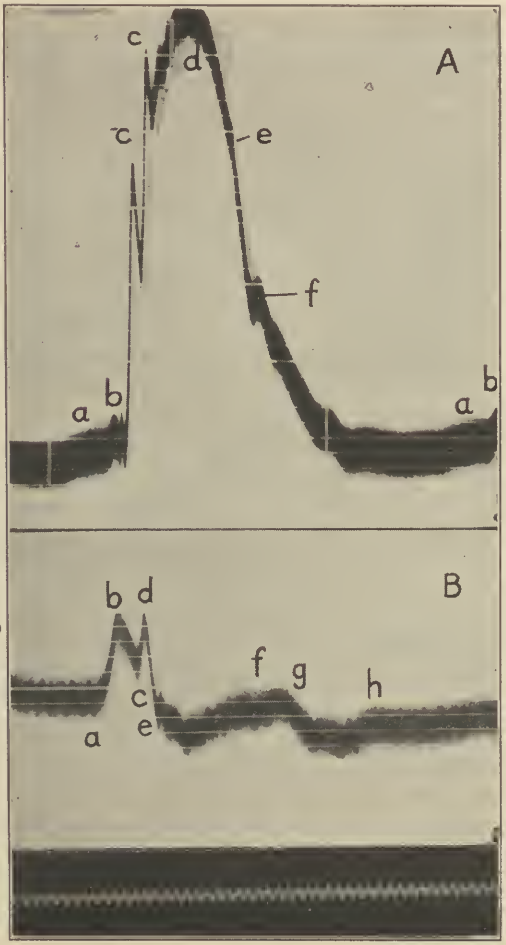

FIG. 22.—Pressure changes in the pulmonary artery (upper) and the right auricle (lower). *Upper record:* *a*, auricular wave; *b*, preliminary vibrations; other letters as in Fig. 20. *Lower record:* *a–c*, auricular systole; *c–d–e*, early systolic vibration; *f*, small notch at end of systole; *g*, early diastolic fall, opening of tricuspids; *h*, mid-diastolic wave, occasionally present.

phase of the ventricle. Synchronous with the change in contour of the intraventricular curve (Fig. 20, x–x'), the arterial pressure rises sharply (b–c) and falls again (c–c'). This primary wave is due to the sudden ejection which throws the aortic column of blood into vibra-

tion. It is more pronounced in the pulmonary artery, where there may be two primary oscillations (Fig. 22, *A*). During the rest of the ejection period (*d–e*) the curve follows that of the ventricle, since the two chambers now constitute a common cavity. With the onset of diastole the pressure falls rapidly (*e*) with that of the ventricle—a fall that is accompanied by a backward movement of the column of blood. It has been called the *incisura* (Frank). The fall is suddenly checked by the closure of the semilunar valves and is followed by one or several

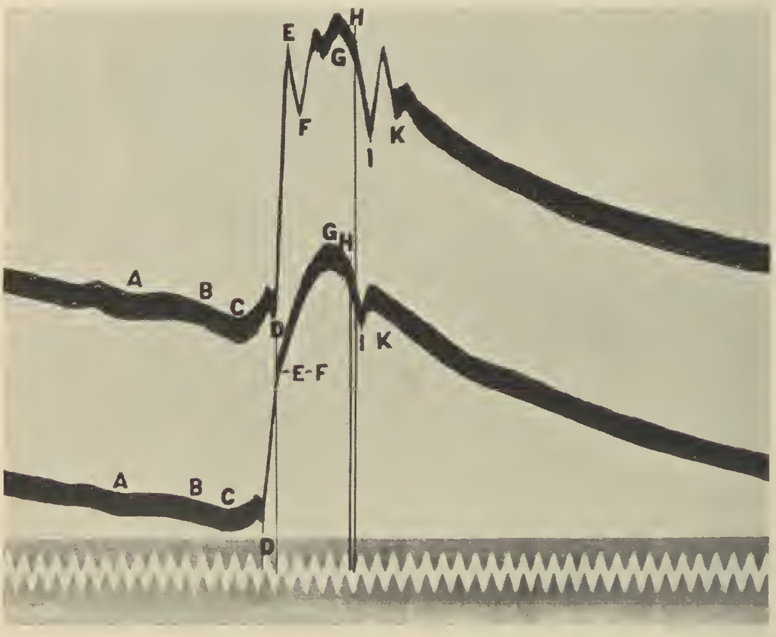

FIG. 23.—Synchronous pressure curves from aorta near semilunar valves (lower) and innominate artery (upper), showing changes in contour of pressure curve in aorta and its immediate branches and variable rate of propagation at different pressure levels. *A–C*, auricular systole; *C–D*, preliminary vibration during isometric contraction; *D–E–F*, primary oscillation; *F–G*, systolic maximum during maximum ejection phase; *G–H*, reduced ejection; *I*, incisura; *K*, after-vibrations becoming larger in innominate. Velocity of transmission at *D–D*, 3.2 meters per second; at *H–H*, 17.6 meters per second.

oscillations due to their after-vibration (*f*). During diastole the pressure falls gradually in the systemic aorta, but more rapidly in the pulmonary circuit (*cf.* Figs. 22 and 23).

In addition to these grosser features, several smaller preliminary vibrations may be present. They are found both in the pulmonary and systemic curves (*cf.* Fig. 22, *A*, with Fig. 23). The first wave (*A B*, Fig. 23; *a*, Fig. 22, *A*) occurs during auricular systole, the second shorter vibration (*C D*, Fig. 23, and *b*, Fig. 22, *A*) falls during the steep

rise of intraventricular tension preceding ejection. The summit of the pressure curve may come early or late during ejection, depending on how rapidly a balance is struck between velocity of systolic ejection and peripheral flow from the arterial system.

The same pressure variations occur in the root of the aorta near the semilunar valves (Garten, Piper, C. Tigerstedt, Wiggers), with the exception that the pronounced primary vibration *D, E, F* (Fig. 23) is greatly reduced or only barely indicated. It is quite apparent that this vibration is artificially produced by the rebounding blood in the subdivisions of the aorta and does not result from cardiac pressure changes.

Intra-auricular Pressure Curves.—The first and chief wave (*a, b, c*, Fig. 22, *B*) is caused by auricular systole. Its amplitude varies with the vigor of auricular systole. At the beginning of ventricular contraction a short positive rise (*c–d*) followed by a negative drop occurs, and then the pressure increases slowly not only throughout systole to *f* but a short while into diastole, *i. e.*, to *g*, when the *A–V* valves open and blood flows into the ventricle. At this point the venous pressure falls more or less; sometimes it is a very distinct drop; at other times it is barely perceptible. Similar changes are shown in Fig. 21. The changes are essentially the same, but of different magnitude in the left and right auricles. The auricular wave of the right auricle definitely precedes that of the left.

THE VOLUME CURVES OF THE VENTRICLES.

As systolic ejection is accompanied by a reduction in the volumes of the ventricles and their subsequent relaxation and filling again increase their volumes, the plethysmographic record of the ventricles supplies a method of studying ventricular filling and ejection in detail.

A record of these volume changes can be obtained by enclosing the ventricles by a plethysmograph or cardiometer and communicating the variations in volume to a suitable recorder. As the volume of the ventricles decreases during systole the recording lever descends, and as it increases during diastole it ascends. The method was introduced by François-Franck and Tigerstedt, and since its more practical development by Y. Henderson has been extensively employed (de Heer, Patterson, Piper and Starling, Rothberger, Straub, Wiggers and Katz, etc.).

The most satisfactory cardiometer consists of a glass sphere containing an opening with a small flange over which a rubber diaphragm is tied (Fig. 24, *A*). In this is cut a round opening slightly smaller than the circumference of the cardiac base. After it is applied to the heart the cardiometer must be so supported that the heart itself does not move in and out of the rubber and that no impact from the auricle is imparted to it.

To record the volume changes a variety of instruments have been used. Henderson used a large Marey tambour, 12 cm. in diameter, which was covered by unstretched rubber. Among other apparatus which has been employed to record tracings on a smoked surface may be mentioned the piston recorder, the bellows recorder and the segment recorder. Optical curves have been taken through the use of a soap membrane spread over a funnel and directly photographed (Straub) and also by the inscription of the small pressure variations within the system by optical capsules (Patterson, Piper and Starling,

Fig. 24.—Cardiometer (A) and tambour (C) used by writer for recording ventricular volume curves. To take an optical record the slight pressure changes within the large tambour are communicated to a Frank segment capsule (E).

Wiggers and Katz). Finally, mention must be made of volume curves obtained by integration of ventricular tachograms recorded by means of optical capsules (Straub).

The apparatus preferred by the author is shown in Fig. 24. The volume changes within the cardiometer are communicated by tubing 12 mm. internal diameter and 60 cm. long to a tambour 9 cm. in diameter, constructed on the principle of a segment capsule (Fig. 24, C). When this segment recorder is covered by thin rubber dam, smoothly fastened over the surface without stretching, 30 cc displacement causes a pressure variation of 31 mm. of water. By attaching

to the trapezoidal plate pivoting on its chord side a straw lever 12 cm. in length and magnifying three times, a graphic record can be inscribed on a smoked surface. In order to inscribe the systolic ejection as a downstroke, the apparatus must be inverted. Except for the distortion incurred by arcs of levers, such records are very reliable as to details.

In order to relate the volume changes to pressure curves which cannot be inscribed with accuracy on smoked surfaces, it is sometimes necessary to record optical volume curves as well. To accomplish this, the slight pressure variations within the large capsule can be communicated to a Frank segment capsule (Fig. 24, *E*). This apparatus fulfils all the demands made upon it and is suitable either for graphic records on smoked paper or optical tracings, or what often proves desirable—both together.

Critique of Apparatus.—It is, of course, necessary that the apparatus employed should be adequate to record variations in ventricular volumes accurately and at the same time not interfere with the natural beat of the heart. Consequently, the apparatus and technic must fulfil the following requirements:

1. The rapid volume changes taking place within the cardiometer must be accurately picked up by the recorder. Hence, it is necessary to consider the efficiency of recording devices. The principles according to which efficient volume recorders should be constructed are well understood (*cf.* Brodie, Henderson, Straub). Fundamental emphasis is laid by investigators on two important requisites: (1) The necessity of avoiding more than minimal variation of pressure within the system, and (2) the maintenance of an adequate inherent vibration frequency. Two types of apparatus, as Brodie points out, have been utilized: (*a*) *True volume recorders*, in which the internal pressure variations are very slight, and (*b*) tambours, in which volume changes are translated into pressure changes and the latter recorded. Most experimenters, seeking to avoid what is usually regarded as a deleterious effect of negative pressure variations about the ventricles, have endeavored to use *true volume recorders.* With the possible exception of the soap-bubble device suggested by Straub and later found impracticable by him, it is not possible to construct recorders which qualify as regards inherent frequency.

The author is of the opinion, however, that the development of moderate negative pressure variations about the ventricles during the heart cycle is not detrimental to their normal action; that, on the contrary, it is quite normal and favorable. The heart is naturally enclosed within a plethysmographic cavity, the chest, and every volume change is accompanied by pressure variations about the ventricle (*cf.* Fig. 25). Since actual measurement shows that, in addition to the negative pressures exerted on the ventricles during inspiration and expiration, each ventricular systole itself causes an intrathoracic pressure

change ranging from 9 to 20 mm. of water, natural conditions are but reduplicated when similar changes occur about the ventricles in a cardiometer. If such an apparatus is used we are in a position to

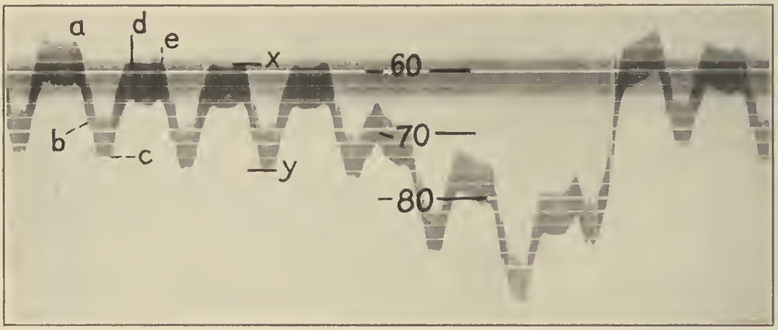

FIG. 25.—Cardiac and respiratory variations of intrathoracic pressure. Cardiac contractions caused a total decrease in pressure (x–y), equal to 16 mm. of water, when the total respiratory variation equalled 63 mm. a–c, ventricular systole; c–d, rapid inflow; d–e, diastasis.

improve its vibration frequency. Since the systolic ejection is probably the most rapid phenomenon recorded and its duration is rarely less than 0.1 second, an instrument with an inherent frequency of 15 per second is probably quite adequate.

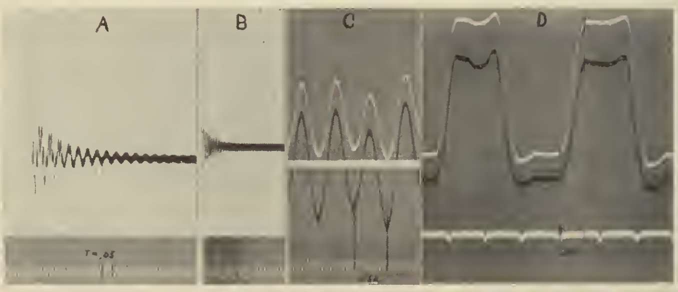

FIG. 26.—Four segments of records illustrating different dynamic tests of volume recorders (one-third actual size). A, test of vibration frequency of closed system ($N = 20$); B, vibration test of segment capsule ($N = 100$); C, correspondence between piston movements (white) and volume recorder (black), when variations of strokes exceeded 375 per minute (optically recorded); D, similar correspondence of slower and more extensive volume changes, establishing deflection time (0.1 second), absence of overshooting and delay in conduction. (After Wiggers and Katz.)

In order to be certain that an apparatus has the required efficiency it is necessary to show: (a) That the inherent frequency is above 15 per second; (b) that the deflection time is less than 0.1 second; (c) that no overshooting or lag occurs; and (d) that it is capable of reacting faithfully to volume changes occurring at rates greater than that of

the heart to be studied. The segment tambour has these requisites, as shown in the dynamic tests incorporated in Fig. 26.

2. The cardiometer volume changes must correspond to those of the cardiac chambers, or, if disturbed by mechanical factors, the latter must be discountable in records. The mechanical factors that may complicate volume curves and thus render them inaccurate are: (*a*) Variations in the blood content of the ventricular walls; (*b*) impacts of auricular systole on the rubber diaphragm; (*c*) position changes in the cardiac base at the beginning of systole and diastole; (*d*) bulging of the *A–V* valves at the beginning of ventricular systole; and (*e*) difficulty of excluding a portion of the pulmonary conus. (For details *cf.* Wiggers and Katz.)

We may, therefore, conclude that while it is quite possible to record directly and accurately such volume changes as occur within the plethysmograph, these changes may not represent a true picture of intraventricular volume changes. The accidental distortions thus produced can, however, be detected on the volume curves and discounted with sufficient accuracy to permit of their use in studies of contour changes. (*cf.* Wiggers and Katz.)

The Accidental Distortions of the Systolic Stroke.—Many misinterpretations of volume curves have been due to the fact that the beginning and end of systolic ejection were not carefully established. In order to check the accuracy of volume changes during systolic ejection, the aortic pressure curves near the semilunar valves must be simultaneously recorded. This is important not only because it is thus possible to determine the beginning and end of ejection precisely, but also because the contour of the volume curve can really be predicted from changes in the gradients of the pressure curves. If the volume and pressure curves agree, direct proof of the accuracy of the volume curve is given; if they do not show such a correspondence their accuracy must be questioned.

It is obvious that with the beginning of the rise of aortic pressure the volumes of the ventricles must decrease. Precise time relations show, however, that this is rarely the case. More commonly the ventricular volume curves either remain unchanged (Fig. 27, 3d beat) or increase slightly during the early moments of ejection (Fig. 27, 2d beat). In the latter case the curves develop a small peak which is also indicated in many published records of other investigators. This slight increase in volume has usually been interpreted as taking place during the isometric period, being frequently held to indicate a pull of the papillary muscles on the *A–V* valves (Straub). Katz and the author found, however, that this notch only rarely precedes, but usually comes at the onset of ejection. Experiments indicate that this is an accidental phenomenon, due to a slight systolic thrust of the heart into the cardiometer.

It is quite obvious that the volume changes recorded during the

isometric phase or during the very beginning of ejection cannot accurately represent actual volume changes in the ventricles. If the peak is small, however, it interferes little with the interpretation of the rest of the record; if it becomes broad and large, care must be exercised not to interpret it (as has occasionally been done) as an effect of auricular systole.

A comparison of contours shown by synchronous volume and pressure curves of the ejection curve corresponds exactly to changes in gradient of the pressure curves.

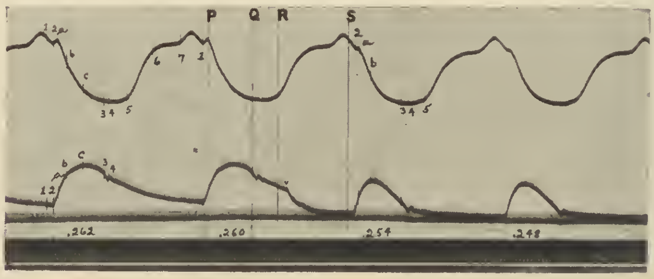

FIG. 27.—Volume and aortic pressure curves during and immediately following aortic decompression; used to illustrate ideal curve in the latter condition and production of an early systolic peak, 2–*a*, due to kick of heart when arterial resistance becomes high (one-third actual size). Small numerals and intersecting lines on curves demarcate the following phases: 1–3, entire systole; 3–1, entire diastole; 1–2, isometric phase (approximately); 2–3, systolic ejection (subdivided into shorter phases, *a*, *b*, *c*); 3–4, protodiastolic phase; 4–5, isometric relaxation phase; 5–6, rapid inflow phase; 6–7, diastasis phase; 7–1, auricular systole phase. Note abbreviation of systolic ejection on decompression. Lines *P–Q* and *R–S* indicate portions of records considered reliable in volume curves. (After Wiggers and Katz.)

Accidental Distortions of Diastole.—Experience has shown that the accidental changes in volume curves during diastole are limited to the early period of diastole before any inflow occurs. Since blood neither leaves nor enters the ventricles at this time, the ventricular volumes do not actually change. This is the case in many records (*e. g.*, Fig. 27). In other instances the only change is a slight increase, possibly due, as Henderson suggested, to the filling of the coronary vessels. Sometimes, as in Henderson's records, this increase is much greater, and the suspicion then exists that the rebound of blood in the pulmonary conus may contribute somewhat to the distortion. Of greater importance, because it readily leads to misinterpretation of volume curves, is a continued decrease in volume during these phases. Without the time relations, such as given by the aortic pulse or heart sounds, the end of systole is readily interpreted as occurring later than it actually does. The cause of this continued decrease during early diastole is probably due to a return of the cardiac base to its diastolic position.

The Nature of Ventricular Ejection and Filling.—When the accidental deformations existing in volume curves are taken account of in a critical manner, it is usually found that the details of ejection and filling, as included between the lines $P\,Q$ and $R\,S$ (Fig. 27), are capable of accurate interpretation, but that the volume changes occurring just before the ejection and at the end of ejection ($Q\,R$) may have to be discounted. As neither filling nor ejection takes place during these intervals, however, this is of no serious moment.

The essential changes occurring during ejection were first clearly described by Henderson and are indicated also in volume curves obtained by de Heer, Straub, Wiggers and Katz. In all cases, as shown in Fig. 27, there is normally an abrupt decrease in the ejection rate at the time that the aortic pressure begins to decline (2–*c* and *c*–3), thus separating systolic ejection into periods when the velocity of ejection is great and when it is much reduced.

A number of investigators, however, have described other variations. Patterson, Piper and Starling report that during the latter phase of ejection the volume curves may be entirely horizontal, indicating that a condition exists in which no blood is expelled (the so-called Rückständige Kontraktion of older writers). These investigators undoubtedly fell into error in that the end of systolic ejection was misinterpreted, the period of horizontal curve probably coming during the early diastolic phases and not during systole (Wiggers and Katz). On the basis of tachogram studies, Straub has come to the conclusion that the velocity of ejection changes several times. Wiggers and Katz have been able to confirm this and, as shown in Fig. 27, the velocity of ejection is uniform during the phase of maximum ejection only when arterial resistance is low and the aortic curve mounts smoothly to a summit (Fig. 27, 3d and 4th beats). When resistance is at or above the normal level we find, contrary to Henderson and in accord with Straub, that the velocity of ejection may change a number of times, depending on the resistance developed in the arteries from moment to moment. Contrary to Straub, we believe it impossible to select any type of variation as normal, there being as many variations of ejection during this phase as there are types of pressure curves. Thus, in the first beats of Fig. 27 the velocity of ejection is very rapid during the primary elevation of aortic pressure, *a*–*b*, and is somewhat reduced as the pressure curve gradually reaches a summit, *b*–*c*.

Strictly speaking, therefore, the ejection process under normal conditions probably occurs in three stages, that is to say, at the opening of the semilunar valves a large quantity of blood is expelled with great velocity. This is soon halted slightly, but ejection still proceeds beyond mid-systole with very considerable velocity, and finally toward the end of systole the rate of ejection shades off gradually, but never entirely ceases.

The diastolic filling in normal hearts was also first described with accuracy by Henderson and is illustrated also in records published by de Heer, Wiggers and Katz and others. The chief changes are shown in Fig. 27. As soon as the A–V valves open, filling occurs rapidly, as indicated by the rapid upstroke, 5–6. This is followed by a period of decreased inflow and occasionally an almost complete stasis indicated by the nearly horizontal or gradually mounting line from 6–7. This is followed by a further increase, 7–1, due to auricular systole.

An essentially different mode of filling is indicated by the records of other investigators, notably Patterson, Piper and Starling. They dissent from the view that a phase of relatively slow inflow or diastasis exists, believing that filling continues with unabated velocity until the end of diastole. As has been frequently pointed out (Henderson, Wiggers), such effects occur only when the heart is beating rapidly, so that no time for diastasis is available, or when the venous pressures are abnormally high in relation to cardiac relaxation, and may, therefore, not be regarded as normal.

According to volume curves, such as are shown in Fig. 27, auricular systole contributes relatively little to ventricular filling. Straub, Patterson, Piper and Starling, as well as Gesell, dissent from this view and hold that auricular systole contributes a considerable increment. Katz and the author have given this question the most recent consideration. On the basis of our volume curves, we concluded that, in his zeal to emphasize the importance of early diastolic filling, Henderson probably underestimated the part played by auricular systole. We found that the volume contributed is inconstant, figures ranging from 18 to 60 per cent of the total filling, with an average of 35 per cent. It is apparently dependent: (*a*) On the time that auricular systole comes in diastole; (*b*) on the completeness with which the ventricle has already been filled at the time of auricular systole; and (*c*) on the vigor of auricular systole. Other things being equal, an auricular systole coming during or soon after the early diastolic inflow phase contributes a considerable amount of blood. This agrees also with the records of Straub and de Heer. Coming at the end of a long diastasis, it is able to contribute little more, as held by Henderson. These records also corroborate an observation of Gesell, viz., that to be effective the As–Vs interval must not be too long. Frequently a considerable volume is injected during the dynamic phase of auricular systole, but if the As–Vs interval is sufficiently long the curve returns to its previous level, indicating a back flow of blood toward the auricle (Fig. 27). In such cases auricular systole cannot be said to aid ventricular filling. If this interval is shorter, time for this back flow of blood is lacking and the contribution of auricular systole is permanent. On the whole, however, our records show that even in slower beats the auricle contributes somewhat more than Henderson has generally held.

The Temporal Relation of Volume and Pressure Curves.—The Phases of the Cardiac Cycle and the Sequence of Dynamic Events.— Having determined accurately the pressure changes of the cardiac chambers and the aorta (Fig. 21), as well as the volume changes of the ventricles (Fig. 27), it is possible to superimpose these curves, as

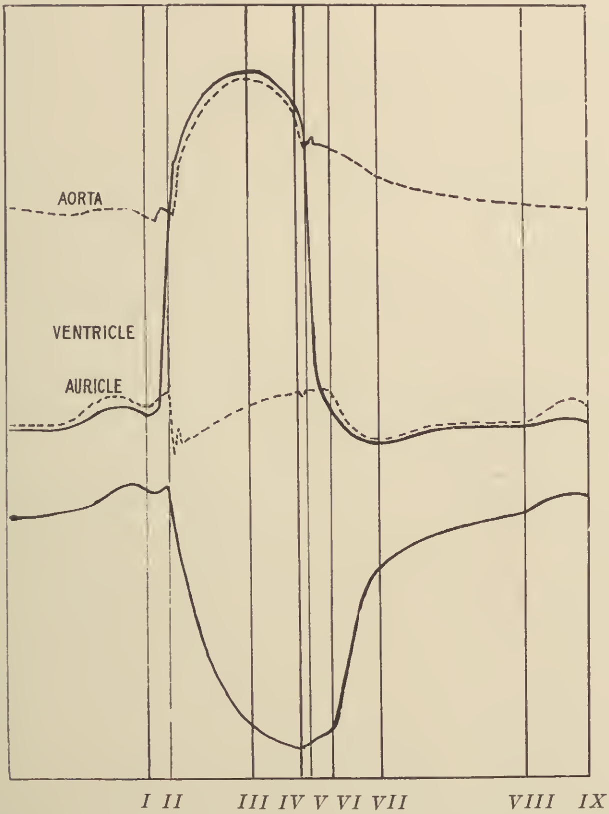

FIG. 28.—Superimposed curves of pressure changes in ventricle (heavy line); aorta (upper dotted line) and auricle (lower dotted line), together with volume curves of ventricles (lower solid line). *I–IV*, systole; *IV–IX*, diastole; *I–II*, isometric contraction phase; *II–III*, maximum ejection phase; *III–IV*, reduced ejection phase; *IV–V*, protodiastolic interval; *V–VI*, isometric relaxation phase; *VI–VII*, rapid inflow; *VII–VIII*, diastasis; *VIII–IX*, auricular systole.

shown in Fig. 28, and from them deduce the details of the cardiac mechanism. While the detailed conformation of these curves alters under experimental conditions, as will be later pointed out, and varies also in different animals, the curves shown in Fig. 28 indicate fairly well their character and time relations under normal conditions applying to man when the heart rate does not exceed 80 per minute.

Phases of Ventricular Systole.—At the onset of ventricular systole the pressures within the auricle and ventricle are approximately equal. At this time, as indicated by the experiments of Dean, the *A–V* valves are in the act of floating into apposition. As Henderson and Johnson suggest, this movement is probably initiated by the sudden cessation of the jet when the peak of the presystolic auricular wave is reached. The first elevation of intraventricular pressure firmly closes these valves and the intraventricular pressure then rises steeply (*I, II*). As the semilunar valves are also closed during this rise of intraventricular pressure a bulging of both semilunar and *A–V* valves takes place and accounts for the slight elevation of auricular pressures as well as the small initial wave on the arterial pulse (Fig. 28). Frequently the latter is preceded, however, by a negative drop, due, as direct records show, to traction of the ventricle on the large vessel. As the volume curves show no true changes in volume and both valves are closed, the ventricle contracts as an isometric muscle, and consequently this phase has been designated by the author as the *isometric contraction phase.*

Other names have also been applied to this period. Thus, Chauveau and Marey, Hürthle and von Frey speak of this as the "Anspannungzeit," a phrase which has usually been translated into English as "the period of rising tension," or also the "presphygmic period." The latter term is unfortunately inaccurate, since there is a well-marked sphygmic oscillation on the arterial pressure curve.

As soon as intraventricular pressure exceeds intra-aortic the semilunar valves open (*II*) and, as indicated by the steep descent of the volume curve, a rapid ejection of blood takes place into the aorta. This causes the aortic pressure to rise rapidly and the throw of the blood volume causes the primary vibration. As the ventricular muscle shortens during this ejection a sudden descent of the cardiac base takes place and causes an abrupt fall in auricular pressure, followed occasionally by one or two after-vibrations. After the primary shock of the sudden ejection has passed the pressure curve of the aorta follows that of the ventricle, but naturally remains somewhat lower, which is as expected, for ventricle and aorta now form a common cavity and blood must at all times move from a higher to a lower pressure. For some time, as shown between the lines *II* and *III*, this rapid ventricular ejection continues and the volume ejected is greater than the outflow from the peripheral arterioles (*maximum ejection phase*). As soon, however, as the volume of the systolic discharge decreases, as shown by the more gradual gradient of the volume curves between *III* and *IV*, the systolic discharge no longer equals the peripheral outflow and both the aortic and intraventricular pressures begin to decline (*III* to *IV*). This *reduced ejection phase* terminates the ejection phases of the heart beat.

It has often been pointed out that during this phase of ejection the muscle contracts in approximately isotonic fashion. It differs, however, from the shortening of an after-loaded muscle in that the tension is not absolutely constant. Consequently, Starling has proposed the term "auxotonic," that is, acting under an increasing tension, as expressing the nature of ventricular contractions during the ejection phase. This phrase is also, however, not quite descriptive of the dynamic conditions of the normal heart, which contracts first against an increasing and later against a decreasing load. If a general term is desirable the phrase "allasotonic," that is, acting under a variable tension, would seem more appropriate. On the whole, however, it is just as well to refer to this as the ejection phase.

To summarize, ventricular systole may be divided into: (*a*) An isometric contraction phase; (*b*) a maximum ejection phase; and (*c*) a reduced ejection phase (*cf.* Fig. 29).

Phases of Ventricular Diastole.—At the onset of ventricular relaxation, aorta and ventricle are still in communication (*IV*). The first diastolic event consists in a sharp drop of intraventricular pressure (*IV* to *V*). This causes a slight backward flow in the aorta together with a similar drop of aortic pressure designated as the *incisura*. This fall of aortic pressure, however, is halted by the closure of the semilunar valves, which causes a slight rebound of the blood column and is responsible for the small after-vibrations. This marks the fourth or *protodiastolic phase* of the ventricular cycle. Following the closure of the semilunar valves (interpreted as taking place at *V*), and until the *A–V* valves have opened, the ventricle relaxes without any flow of blood either from or into its cavity. This phase (extending from *V* to *VI*) may be designated as the *isometric relaxation phase*. During the last-named phases of diastole the auricular pressure continues to rise slowly while changes taking place in the volume curves are entirely due to accidental distortions. As soon as the intraventricular pressure has fallen to a level below intra-auricular pressure (*VI*) the *A–V* valves are opened by the difference of pressure, and for the same cause, a rapid ventricular inflow begins. This is made evident by the rapid rise of the volume curves and the sudden fall of auricular pressure. This rapid inflow during early diastole, which is responsible in slowly beating hearts for a large percentage of the total filling, comes to a gradual end when an equalization of pressures in auricle and ventricle takes place (*VII*) or when a subsequent cycle interrupts the filling. This is the sixth phase, which may be designated as the *early diastolic inflow phase*. In long cycles, such as we are considering, when auricular pressure is normal a period of reduced filling or approximate stasis is indicated by the volume curves (*VII* and after), which may be designated after Henderson's suggestion as the *phase of diastasis*. During this interval the ventricle fills gradually, and the auricular and ventricular pressures very slowly rise, the auricular exceeding the ven-

tricular a trifle. During all these diastolic events arterial pressures gradually fall, the rate being determined by the resistance offered to the peripheral flow. Finally, we must recognize the phase of *auricular systole.* Careful studies have shown that intra-auricular pressure rises during the early half of systole but falls during the latter half. This is apparently due to the fact that fractionate contractions of the auricle (*cf.* page 68) are added during the first portion of systole but subtracted during the latter portion. We may, therefore, divide auricular systole into: (*a*) *The dynamic phase,* during which blood is injected into the ventricles, causing a rise of intraventricular pressure and a sudden increase in the ventricular volume, as shown by volume curves, and (*b*) *an inflow phase,* during which the pressure falls in the auricle and during which some blood actually flows into the auricle from the central veins. Furthermore, volume curves indicate that in many cases a slight backflow occurs from ventricle to auricle during the latter phase.

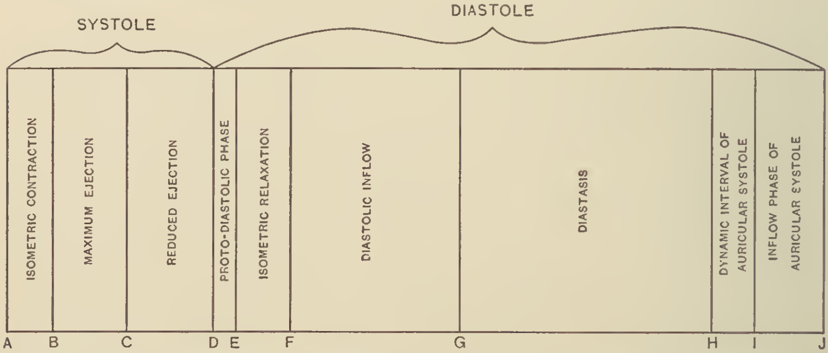

FIG. 29.—Scheme summarizing consecutive phases of cardiac cycle according to dynamic changes.

Summarizing the consecutive phases of diastole, therefore, we may say that it is divided into: (*a*) A protodiastolic phase; (*b*) an isometric relaxation phase; (*c*) a rapid inflow phase; (*d*) a diastasis phase and an auricular systole phase (Fig. 29).

Duration of the Consecutive Phases.—Ever since the duration of auricular systole was estimated by the auricular wave of the right auricular pressure curve as 0.1 second by Chauveau and Marey, this figure has been held to represent the duration of systole in animals and man. Using the criteria previously mentioned (*cf.* page 70), the author found the systole of dogs to vary from 0.077 to 0.14 second, with an average duration of 0.11 second, about one-half of which represents the dynamic interval and the other half the systolic inflow phase. Practically the same figure for total systole was obtained by Lewis, Feil and Stroud.

There is no existing method by means of which the duration of atrial systole may be determined accurately in man. The rise of the *a* wave of the venous pulse, often suggested, represents only the dynamic phase, and there is no evidence of the termination of systole on the descending limb. The *P* wave of the electrocardiogram is probably not concerned with auricular contraction at all. As shown in Fig. 30, the *P* wave begins to rise before intra-auricular pressure (1–2) and the end of systole (4) may not be reached until the entire *R* wave has been completed. If, therefore, the *P–R* interval equals the duration of auricular systole, as Lewis, Feil and Stroud maintain, this is nothing but a fortunate coincidence (*cf.* also Fig. 30).

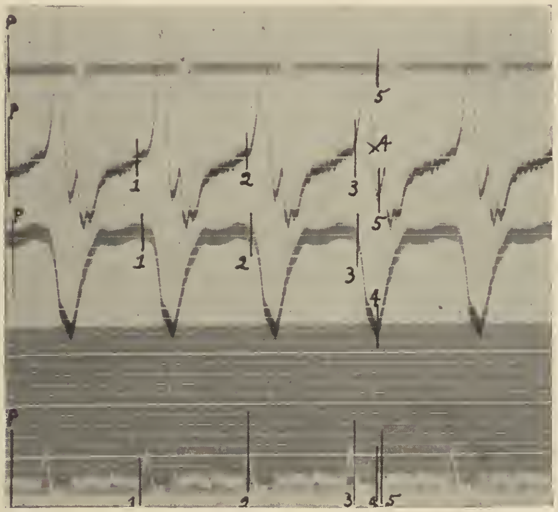

Fig. 30.—Time relations of auricular systole, 2–4, as shown by intra-auricular pressure curve (second) and auricular myocardiogram (third) to waves of the electrocardiogram, Lead II (bottom) and first ventricular sound (upper). Numerals, 1, 2, 3, 4 and 5, synchronous points. (From dog's auricle.)

The following figures have been given for the duration of the isometric phase of ventricular systole by various experimenters:[1]

For horse—Chauveau and Marey, 0.1 second.

For dog—Hürthle, 0.02 to 0.04 second; Fredericq, 0.04 second; Lüderitz, 0.04 to 0.06 second; de Heer, 0.03 to 0.05 second; Wiggers, 0.045 to 0.05 second.

For cats—Piper, 0.05 second.

For rabbits—Lüderitz, 0.02 to 0.04 second; C. Tigerstedt, 0.02 to 0.04 second.

For man (*cf.* also page 206)—Edgren, 0.087 to 0.096 second; Hürthle,

[1] For references to literature, *cf.* Tigerstedt: Physiologie der Kreislaufes, 1921, 1, 209.

0.06 second; Robinson and Draper, 0.07 to 0.085 second; Einthoven and Geluk, 0.06 second; Tigerstedt, 0.05 second; Weitz, 0.035 to 0.084 second; Wiggers and Clough, 0.04 to 0.06 second.

According to Hürthle, in dogs the entire ejection phase varies from 0.178 to 0.195 second. The author obtained the following variations: Maximum ejection, 0.05 to 0.11 second; reduced ejection, 0.063 to 0.144 second.

While the isometric phase is relatively constant under different circulatory conditions, the duration of the ejection phase is subject to considerable variation and is largely responsible for the variation in systole.

The duration of the entire ventricular systole has been determined with approximate accuracy in man by several methods: (1) By establishing the interval between the beginnings of the two heart sounds; (2) by estimating the interval between the rise of the primary wave and of the incisura of the arterial pulse; (3) by measuring the interval between the rise of the *c* wave and the fall of the *v* wave in the venous pulse; (4) by estimating the interval from the *Q* to the end of the *T* variations of the electrocardiogram (Dawson, Bazett). Of these procedures only the first is really accurate, however; the second does not take account of the isometric phase of contraction and is, therefore, probably 0.04 to 0.05 second too short. The third procedure is inexact in that it has the same error as the second, but, in addition, includes the protodiastolic and isometric relaxation phases of diastole. Finally, the electrical deflection intervals do not vary proportionally with mechanical systole even under normal conditions. This has been most conclusively demonstrated by work just completed in this laboratory by Miss Bartos and Burstein.

By these various methods the results shown in the following table have been obtained:

Investigator.[1]	Heart rate ranges.	Ventricular systole.	Method.
Volkmann	84	0.375	Heart sounds.
Donders	74–94	0.327–0.301	" "
Landois	55–113	0.346–0.190	" "
Roos	62–160	0.327–0.202	" "
Weber and Wirth	60–90	0.350–0.280	" "
Weitz	42–105	0.378–0.295	" "
Edgren	70	0.379	" "
Eyster	67–88	0.367–0.322	" "
Thurston	47–128	0.347–0.256	Arterial pulse.
Reckzeh	60–82	0.440–0.350	" "
Lombard and Cope	66–89	0.290–0.236	" "
Wiggers and Clough	60–120	0.330–0.230	Heart sounds and arterial pulse.

Numerous investigators have shown that the duration of systole is dependent on the heart rate. Thus, Wiggers and Clough presented plots of twenty-five normal resting men which indicated that

[1] For references, *cf.* Tigerstedt, Bazett, Katz.

the following general rule applies: Systole has a duration less than 0.25 second when the heart rate is above 100 per minute, averages about 0.25 second at ranges of rate between 80 and 100; ranges from 0.28 to 0.3 second at heart rates between 66 and 80, while it is distinctly longer than 0.3 second when the heart rate is still slower.

Several attempts have been made to correlate the duration of systole with heart rate by the use of formulæ. Thus, Garrod has presented two formulæ which he calculated from the cardiogram and radial pulse. For the former he offered the formula $xy = 20\sqrt{x}$; for the latter $xy = 47\sqrt[3]{x}$. In both x is the heart rate per minute, y the relation of systole to cycle length. Later, Lombard and Cope presented the formula $S = \frac{60}{K\sqrt{R}}$ to determine the length of systole from heart rate, S being the duration of systole, R the heart rate per minute and K a constant varying for position of body, etc. They used the carotid pulse to obtain their data. K they found to be 28.5 for standing postures, 26 for sitting and 25 for lying down. Katz has converted this formula into terms of cardiac cycle $S = \frac{7.8\sqrt{C}}{K}$ or for the lying posture when $K = 25$, $S = 0.31\sqrt{C}$. Waller has calculated the duration of systole according to a similar formula, $S = K\sqrt{\text{cycle}}$, K having a value of 0.343. Bazett calculates systole from the electrocardiogram according to the formula $S = K\sqrt{\text{cycle}}$, where $K = 0.37$ for men and 0.4 for women. Fridericia uses the formula $S = 8.22\sqrt[3]{p}$ where p is the duration of the electrical heart cycle in the sitting posture.

The duration of the separate diastolic phases have apparently not generally been considered of sufficient consequence to merit calculations. The author has established the following figures in dogs: Protodiastolic phase average, 0.022; isometric relaxation, 0.048 to 0.05; rapid inflow, 0.045 to 0.06 second. On the basis of optical venous and arterial tracings, Burstein, in my laboratory, has recently calculated these intervals in man with the following results: The protodiastolic phase averages 0.038 second; the isometric relaxation phase ranges from 0.037 to 0.136 second and averages 0.076 second; the rapid inflow phase ranges from 0.055 to 0.178 second and averages 0.113 second. Comparison of the results on anesthetized dogs and man indicates two essential differences: (1) A greater variability in the phases as determinable in man, and (2) in general, longer average durations in man.

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de Heer: Arch. f. d. gesam. Physiol., 1912, **148**, 1 (*pressure and volume curves of ventricles*).
Frank: Ztschr. f. Biol., 1903, **44**, 445; 1904, **45**, 464; 1906, **48**, 489; 1908, **48**, 309; 1916, **53**, 545 (*theory of manometers, optical manometers*).
Frank: Ztschr. f. Biol., 1905, **46**, 478 (*pressure curve in central arteries*).
François-Franck: Travaux du lab. du Marcy, 1877, **3**, 321; Arch. de physiol., 1890, **22**, 395 (*volume curves of ventricle*).
Garten: Ztschr. f. Biol., 1915, **66**, 23 (*electrical recording manometer, pressure curves of aorta and ventricle*).
Garten and Weber: Ztschr. f. Biol., 1915, **66**, 83 (*pressure curves in auricle—open and closed chest*).
Gesell: Am. Jour. Physiol., 1911, **29**, 32; 1915, **38**, 404; 1916, **39**, 239 (*auricle and ventricle filling—criticism of volume curves*).
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Henderson and Barringer: Ibid., 1913, **31**, 288, 353 (*volume curves of ventricle, critique*).
Patterson and Starling: Jour. Physiol., 1914, **48**, 357 (*volume and pressure curve, perfused dog's heart*).
Piper: Arch. f. Physiol., 1912, p. 343; 1913, pp. 331. 363, 385; 1914, p. 365 (*trocar-manometer; pressure curves in auricle, ventricle and arteries*).
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Tigerstedt, R.: Ergebn. der Physiol., 1907, **6**, 269; Physiol. des Kreislaufes, 1921, 2d ed., **2**, 103 (*pressure curves—earlier literature—review*).
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Articles Dealing with Phases of Cardiac Cycle.

Bazett: Heart, 1920, **7**, 353 (*ventricular systole, duration of*).
Burstein: In press (*duration of diastolic phases*).
Chauveau and Marey: Mémoires de l'acad. de méd., 1863, **26**, 289 (*phases of ventricular systole*).
Fridericia: Acta med. Scandinav., 1920, **53**, 469; 1920, **54**, 17 (*formula for duration of systole*).
Katz: Jour. Lab. and Clin. Med., 1921, **6**, 291 (*duration of ventricular systole*).
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CHAPTER IV.

THE EFFICIENCY AND ADAPTABILITY OF THE HEART.

Under a variety of conditions, both normal and abnormal, the heart is required to adapt itself to altered circulatory conditions. The volume of venous blood returned to the auricles may increase or decrease, and the arterial resistance against which blood must be ejected may alter. In association with or independent of these changes in rate or rhythm may occur and, finally, the inherent contractile functions may be stimulated or depressed. It is, therefore, important, in order to untangle such a combination of effects to study them, as far as possible, separately.

Influence of Variations in Venous Return.—It is generally accepted as demonstrated that when the volume of blood returned to the heart is decreased the systolic discharge of both ventricles is also reduced (*cf.* page 580). Opinions have differed, on the other hand, as to whether a progressively augmented systolic discharge occurs when the venous return exceeds normal. Henderson, in his earlier studies, found that the volume curves at constant heart rates remained superimposable even when auricular filling pressures are slightly reduced below normal, and consequently postulated that when auricular filling pressures are augmented by an increased venous return they are incapable of further affecting the rate of ventricular inflow and consequently the systolic discharge. Henderson, therefore, believes that a pressure of 50 mm. saline in the right auricle is critical for maximum systolic ejection.

In discussing this question it is essential to bear in mind that when the heart is surrounded by a pressure less than atmospheric, as is the case in the closed chest, *the pressure effective in filling the ventricle is not the pressure actually measured in the auricle but the algebraic difference between intrathoracic and intra-auricular pressures* (measured, to be exact, at the *A–V* valves immediately before ventricular diastole). This pressure difference has been termed the *effective pressure* (Henderson and Barringer). Thus, if a venous pressure of +10 mm. of water and an intrathoracic pressure of −40 mm. exist, then the effective pressure is 50 mm. of water.

As the effective right auricular pressure in locally anesthetized dogs varies from 43.6 mm. saline in expiration to 63.1 mm. during inspiration (Wiggers), it is obvious that the ventricles are normally working at maximum efficiency. In studying this question on the perfused

cat's heart, Henderson and Prince subsequently concluded that while this is correct for the right ventricle the left is able to increase its discharge when auricular pressure mounts to 150 mm. saline. While this may operate, as the authors suggest, to prevent pulmonary congestion, it is obviously not a "factor of safety" as regards pumping increased venous volumes from the venous to the arterial side, for the left heart can pump no more than the right heart is able to deliver to the left auricle. The only conclusion that may, therefore, be arrived at, according to this attitude, is that an excessive return above normal must be accommodated in and engorge the large veins and liver unless an acceleration of the heart takes place.

A great deal of evidence has accumulated, however, which indicates that this is not the case. Both R. and C. Tigerstedt have shown, by stromuhr experiments, that the minute volume is promptly increased after saline infusion or blood transfusion, and similar results are also indicated by the work of Stewart. Further, during excessive exercise, when venous pressure is elevated (Hooker), and in spite of the fact that the heart is greatly accelerated, each stroke apparently causes a much larger discharge than normal (Krogh, Zuntz, Meek and Eyster). Patterson, Piper and Starling, moreover, have shown that at constant heart rate and constant arterial pressures the ventricles of a "heart-lung preparation" are capable of responding by progressively increasing systolic discharges until the right venous pressure equals as much as 200 to 250 mm. saline. Obviously, the critical level established by Henderson is much exceeded in these experiments.

If the heart is indeed capable of thus increasing its systolic discharge, however, there must be some evidence of an altered amplitude and contour of the volume curves and intracardiac pressure curves. Krogh, on theoretical grounds, has attempted to show the changes that must be involved. It remained for Patterson, Piper and Starling and Straub, independently, to determine the changes in a "heart-lung preparation." All these observers found that as the venous pressures increased the right ventricle became more and more distended in diastole, and that the systolic discharge increased progressively as the venous pressure rose. Henderson, however, takes exception to such experiments, explaining that while they indicate what the heart *can* do under unnatural conditions it may not be an index as to what it actually *does do* in the intact circulation. This argument is no longer valid, however, for Katz and the author have recently reported identical changes in the intact heart. Typical changes are shown in Fig. 31.

In the experiment shown in the upper series the vagi nerves were uncut, consequently the heart slowed and venous pressures mounted rapidly. In the lower series the vagi nerves had been cut, the cardiac cycle was practically unaffected and venous pressure rose slowly. Such records confirm, in the main, the results obtained by Starling and

his collaborators. They clearly demonstrate that the systolic discharge increases progressively, as venous pressures are increased step by step to levels far exceeding those set by Henderson and his collaborators as "critical." The limit of response was not reached until pressures ranging in various animals from 250 to 310 mm. were attained. Above these levels decompensation and decreased discharge occurred. As the venous pressure increased the ventricles dilated. The diastolic volume was affected more than the systolic, accounting for the increased stroke. These changes occurred regardless of whether aortic diastolic pressure remained unaltered or was somewhat increased.

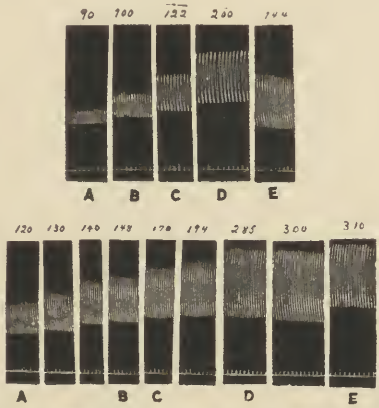

Fig. 31.—Two series of segments, showing progressive increase in diastolic volume and systolic discharge during increase in venous pressure following rapid saline infusion (systole = downstroke). Numerals above segments indicate right auricular pressures in millimeters of saline. Letters below lower segments correspond to similar letters in Fig. 32. Upper series, vagi intact until segment *E;* lower series, vagi divided. (After Wiggers and Katz.)

The diastolic dilatation was more pronounced when the heart coincidently slowed (*cf.* Fig. 31). As shown by comparing segments *D* and *E* of the upper series, this slowing contributed not only to the diastolic distention but to the venous pressure, for both were greatly reduced when the slowing effect was abrogated by vagal section. When no change in heart rate occurred (lower series), systolic discharge increased until a pressure of 285 mm. supervened, remained unchanged as it climbed to 300 mm., but was again reduced when the level of 310 mm. was reached.

The cause of such an increased systolic discharge should also be evident in the volume curves. According to Patterson, Piper and Starling the systolic portion of the curve alter markedly in contour. Their curves, which at low venous pressures were divisible into three phases (rapid ejection, retarded outflow and secondary increased ejection), became smooth and steeper as venous pressure increased.

There is reason to believe, however, that their volume curves were not recorded by adequate apparatus and were, moreover, misinterpreted as regards the end of systole. Straub, in an earlier paper, noted an

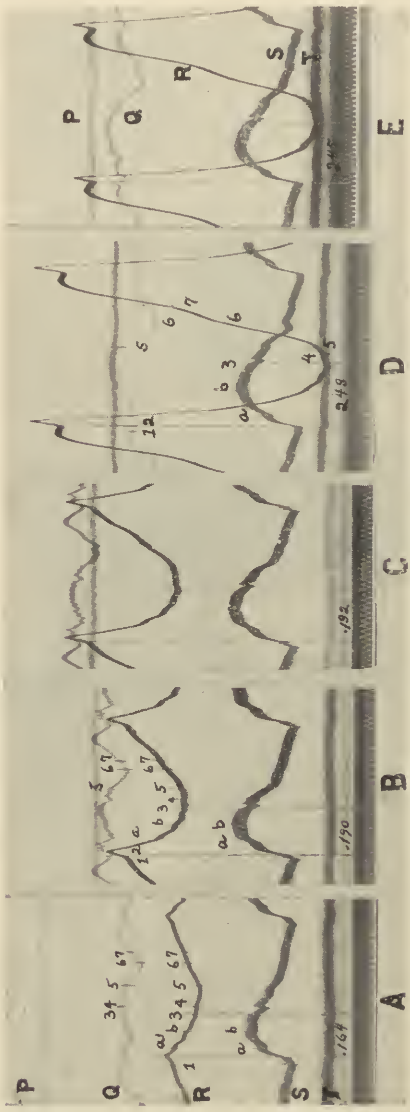

Fig. 32.—Five segments of optical volume curves, *R*. Left auricular pressures, *Q*, aortic pressure, *S*, from experiment taken under different venous pressures (one-half actual size). Letters correspond to similar letters in lower series of Fig. 31. *P*, base line for left auricular pressure; *T*, base line for aortic pressure. Time is 0.02 second. Numerals same as in Fig. 27. Observe progressive increase in duration of ejection phase (figures above tuning fork), increased steepness of both systolic ejection (2–3) and more rapid diastolic filling (5–7), changes in left auricular and aortic pressures. Further description in text. (After Wiggers and Katz.)

increased steepness of the latter part of ejection as the only effect. In curves derived from integration of tachograms he subsequently found a steeper gradient in all phases of ejection. Both observers found a

more rapid diastolic filling, Straub mentioning, however, that in all cases auricular systole contributes about 60 per cent to total ventricular filling. No changes in the duration of systole were noted by Patterson, Piper and Starling and a slight increase by Straub.

The optical records obtained by the author and Katz show significant changes. In Fig. 32 are shown five segments corresponding to the drum records of Fig. 31, and in Fig. 33 are three series of transcribed records from other experiments.

They show that the increased systolic discharge was accomplished in part through an increase in velocity of ejection, in part, however, by a prolongation of systole. When an increase in the velocity of ejection occurred it affected not only the earlier phase of maximum ejection, 2–*a*, but also the gradient of the reduced ejection phase, *b*–3 (Fig. 32). These changes in the details of ejection are reflected both in the pulmonary and aortic pressure curves. In both circuits the pulse pressure increased, the gradient of primary rise was steeper and systolic ejection was prolonged, the maximum ejection phase being especially increased. Incidentally, such curves as Fig. 32 indicate no elevation of diastolic pressure—in fact, during the higher infusions it began to decrease slightly, thereby demonstrating clearly that it is quite possible, in intact animals, to vary venous pressures without affecting heart rate or arterial resistance.

A comparison of curves (Fig. 33) as regards the superimposability of their systolic portions shows that especially in the lower ranges of venous pressures the systolic strokes do not coincide but become steeper. In the higher ranges (*e. g.*, 160 to 300 mm. in *C* 288, *IX*, Fig. 33) the gradient often remained the same, making the systolic strokes quite coincident. While, in such cases, the systolic strokes at the lower pressures are segments of the more extended strokes at higher levels, the changing length of systole is in no sense a function of diastolic length but of the rate of venous filling.

With diastole unchanged (*C* 290, Fig. 33), or even shortened during infusion (*C* 288, Fig. 33), it is obvious that the greater discharge must be due to an increased rate of filling. All transcribed as well as original records show that this was the case. At no two venous pressures above 60 mm. were the diastolic portions of the volume curves superimposable. The increased rate of diastolic filling took place irrespective of whether or not the dominant heart cycle included a diastasis phase.

A study of the separate filling phases of diastole (viz., early diastolic inflow 5–6, diastasis 6–7 or auricular systole 7–1) shows that each phase shared in the greater inflow. The diastasis flow, which was very gradual at venous pressures near 60 mm., became progressively steeper as venous pressures mounted, and a casual inspection of drum records gives the impression that the rapid inflow continued uninterruptedly throughout diastole. Careful inspection of optical tracings

shows a distinct change in gradient (*C* 288, *IX*, Fig. 33) at the beginning of diastasis.

As regards the relative filling during the early diastolic inflow phase and during auricular systole, actual computations showed that each phase shared about equally in the increase. Thus, actual calculations of curves *D* and *R* in experiment *C* 288, Fig. 33, showed that the auricular systole contribution increased from 50 to 54 per cent while the early diastolic inflow increased from 30 to 36 per cent of the total filling. The greater rate of inflow during the early diastolic inflow phase was undoubtedly due to the greater venous pressures occurring at the moment of opening of the *A–V* valves.

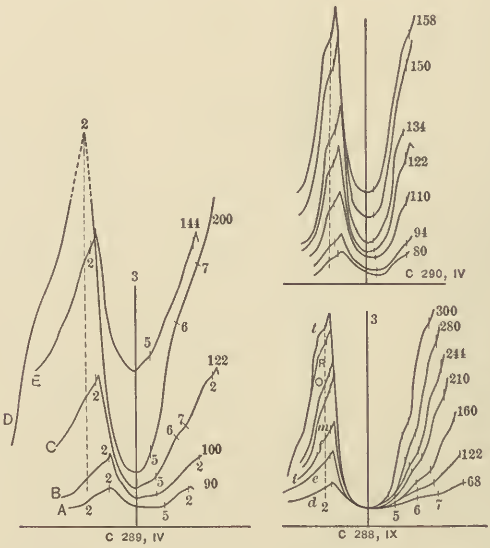

FIG. 33.—Three series of transcribed optical volume curves obtained during increasing venous pressure, showing lack of superimposability of ejection and filling curves as well as prolongation of systolic ejection phase. Exp. C 289, *IV*, from optical curves of Fig. 32. (After Wiggers and Katz.)

We may conclude that the greater diastolic inflow is due: (*a*) In rapidly beating hearts to an increased rate of filling during both the early inflow phase and during the auricular systole phase; (*b*) in slowly beating hearts having a diastasis phase of some duration to an additional increase in rate of filling during diastasis as well.

While such observations refute completely Henderson's contention that the contour and amplitude of the volume curves are incapable of changing, the question may still be raised whether such a degree of distention is possible in hearts intact within the restraining pericardium. The author is under the impression that the snugness of the pericardial

sac has been somewhat exaggerated, and Kuno has shown that it aids rather than prevents the expulsion of larger volumes. Such an objection is apparently negatived by experiments previously reported by the author in animals with thorax intact. In such experiments optical pressure curves in the arteries correspond in every essential with those shown in Fig. 32—the pressure curve always augments in amplitude and the duration of systole increases. This increase in ejection is entirely due to a lengthening of the ejection phases, the isometric phase in fact shortening slightly (*e. g.*, from 0.04 to 0.028; 0.055 to 0.04, etc.). Finally, Meek and Eyster have recently shown by means of instantaneous Roentgen-ray exposures that a similar increase in diastolic volume is obtained in the intact dog's heart when venous pressures are increased by saline infusion up to 150 mm. of saline.

We may, therefore, conclude *that the heart is capable of pumping out larger volumes when venous return is increased, and that this is made possible by an increased rate of filling during early diastolic inflow during diastasis as well as during auricular systole. In order to eject this larger volume the velocity of output is increased and the period of ejection is lengthened.*

Finally, it remains to discuss the fundamental dynamics by virtue of which this more vigorous systolic discharge is made possible. The mere fact that the heart fills to a greater degree does not of itself explain why the increased volume is efficiently expelled during systole. To effect this a more vigorous muscular contraction must occur as a result of some physiological mechanisms. In his studies of the dynamics of the frog's heart, Frank has shown that the vigor of ventricular contraction is determined by the diastolic volume previous to contraction. As every increase in the diastolic volume is accompanied by an increase of tension just previous to diastole, this investigator concluded that the height of the *initial tension*, as the pressure at the beginning of systole is termed, governs the vigor of contraction. The author has also found that every increase or decrease in volume of blood returning to the right heart affects similarly the initial tension, height and contour of the right ventricular pressure curve.

This is shown by the series of curves in Fig. 34. As the auricular pressure decreases, the curve gets lower. The steepness of the isometric limb becomes less; the contour of the ejection period changes; the onset is indistinguishable from the isometric rise and the top is quickly reached. The descending limb of the ejection period merges imperceptibly with the diastolic fall, giving the curve a very simple and rounded contour.

These experiments were the first to indicate that the laws derived by Frank from a study of the frog's heart apply also to the naturally contracting mammalian ventricle. In brief, the conclusion seemed justified that the gradient of the isometric pressure rise as well as the systolic pressure maximum are determined by the initial tension

as long as marked changes in arterial resistance or alterations in the inherent contractility of the heart are not produced. In the meantime, experimental evidence has been accumulating which indicates that in skeletal muscle it is not the initial tension but the initial length of muscle fibers which determines the magnitude of energy production (Blix, A. V. Hill). In comparing volume and pressure curves during progressive stages of increased inflow, Patterson, Piper and Starling found that the initial tension in the left ventricle does not increase. They, therefore, concluded that the initial tension is not the fundamental factor determining greater efficiency, but this is entirely a function of initial tension, that is to say, in the case of the ventricles a function of diastolic volume.

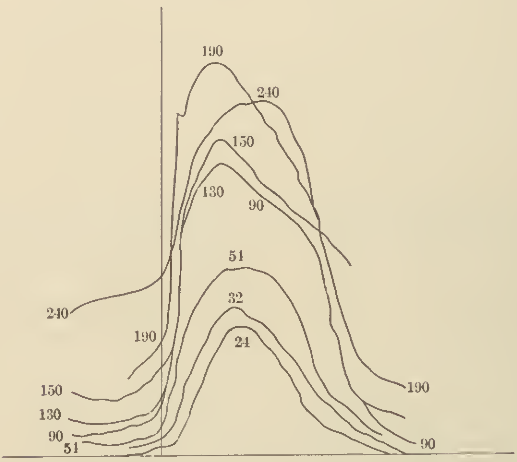

FIG. 34.—Effect of auricular pressure on the initial tension and contour of the pressure curve of the right ventricle. Numbers refer to auricular pressure in millimeters of water.

Subsequent work has apparently been contradictory. Straub interprets his work as indicating that initial tension is a primary factor. Gesell suggests that while both initial tension and initial length may under different conditions determine the ventricular efficiency, the surface-volume relations must also be considered. The author has reported that in his extensive experience he has never found an experiment where actually observed or probable increases in diastolic volume failed to be associated with an increase in initial tension as well. Although the bulk of experimental evidence at the present time indicates that changes in initial volume are always accompanied by changes in initial pressure in the normally beating intact mammalian heart, it is premature to conclude that either one or the other is the fundamental factor which determines varied cardiac response when venous return or venous pressures augment. It may with certainty

be said, however, that the increased tension or greater stretching to which the muscle fibers are subjected during augmented filling is the mechanism through which the ventricle is able to eject large systolic volumes and elevate systolic pressure to a higher level when the venous return increases.

The Influence of Increased Resistance.—It is a matter of simple laboratory demonstration that a lightly loaded muscle is able to contract to a greater extent than one that is heavily loaded. According to the same laws, it may be anticipated that a ventricle ejecting blood against a very high resistance is capable of making only a smaller systolic discharge than against a low resistance. Experimental evidence, however, indicates that this is not the case within such limits of pressure increase as are possible in the body, provided the heart is in prime condition. Stromuhr experiments show that, after marked increase of arterial resistance due to adrenalin, the minute volume is only very slightly reduced (R. Tigerstedt), while after increase of

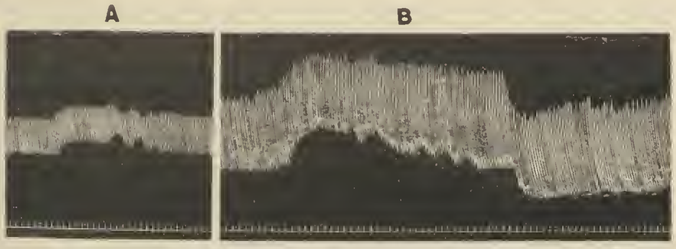

Fig. 35.—Two drum records, showing changes in systolic and diastolic volume changes of ventricles during aortic compression and decompression. *A*, venous pressure rose from 92 to 98 mm. saline; *B*, from 132 to 160 mm. saline. Downstroke systole. (After Wiggers and Katz.)

arterial pressure, due to stimulation of the splanchnic nerves or spinal cord, the minute volume or systolic discharge may actually increase slightly (C. Tigerstedt). Markwalder and Starling have confirmed these observations by direct measurement of the output on a heart, and later Patterson, Piper and Starling and, independently, Straub, demonstrated similar changes by means of ventricular volume curves in perfused hearts. The diastolic volume increased, due to a retention of blood during the first few beats, but after a stable diastolic capacity was once established, at least as large a systolic volume was ejected as before the increase in resistance. Similar results have been obtained in intact animals by Wiggers and Katz, when the arterial resistance is increased suddenly either by compression of the thoracic aorta or through reflex vasoconstriction (Fig. 35). Obviously each heart has a limit beyond which such effects are no longer obtained and a decreased systolic discharge results, the particular limit of adaptability depending largely on the venous return, the cardiac muscle's condition and

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the coronary blood supply. The mechanisms through which this adaptation occurs have been analyzed through a study of the intraventricular pressure curves and the volume curves of the ventricles.

In studying the intraventricular pressure curves, Patterson, Piper and Starling found that the left intraventricular pressure maximum increases, the pressure gradient is steeper and the duration of systole is prolonged. In some cases the noteworthy observation was made, however, that the initial tension is scarcely affected in the left ventricle. These and other observations led to the conclusion that "in the reaction of the heart to increased inflow and increased resistance the only factor which varies constantly is the diastolic volume of the heart, *i. e.*, the initial length of muscle fibers." The contemporaneous studies of Straub, on the other hand, indicated that not only the maximum

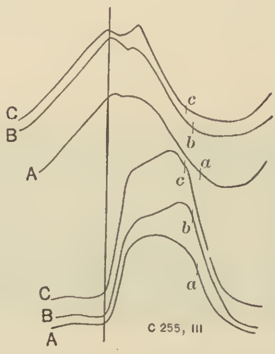

FIG. 36.—Simultaneous volume curves (upper) and pressure curves (lower) from ventricle before, *A*, and after compression of the aorta, *B*, *C*. Curves transcribed and matched at beginning of isometric contraction (vertical line). Letters *a*, *b*, *c*, indicate end of systole. Note: (1) Increase in diastolic volume associated with increased initial tension; (2) abbreviation of systole.

pressure but also the initial pressure was elevated in the left ventricle. Strangely, however, no elevation of either the initial or maximal pressure seems to have occurred in the right ventricle. In subsequent experiments, where both right and left intraventricular pressures were recorded in animals with intact circulation, the author constantly observed an elevation of both initial and maximum pressures in the right as well as in the left ventricle. Such experiments and also those of another series, illustrated in Fig. 36, indicate that an increase in initial tension in the body is never dissociated from an increase in diastolic volume.

The detailed changes in the volume curves have been carefully studied.

Patterson, Piper and Starling found changes in the systolic slope similar to those already analyzed as effects of increased venous return.

They also noted a more rapid diastolic filling rate, due to the increased venous pressures and presented optical curves which indicate a definite prolongation of systole. Straub, in an earlier paper, observed no changes which he ventured to interpret as showing noteworthy deviations in contour. In curves reconstructed from tachograms subsequently reported he found that the steepness of the entire ejection curve increased and the amplitude was greater. Typical immediate effects obtained by Katz and the author are shown in Figs. 36 and 37.

Under such conditions of augmented resistance the duration of systole invariably shortened (Fig. 36). This was not a chance varia-

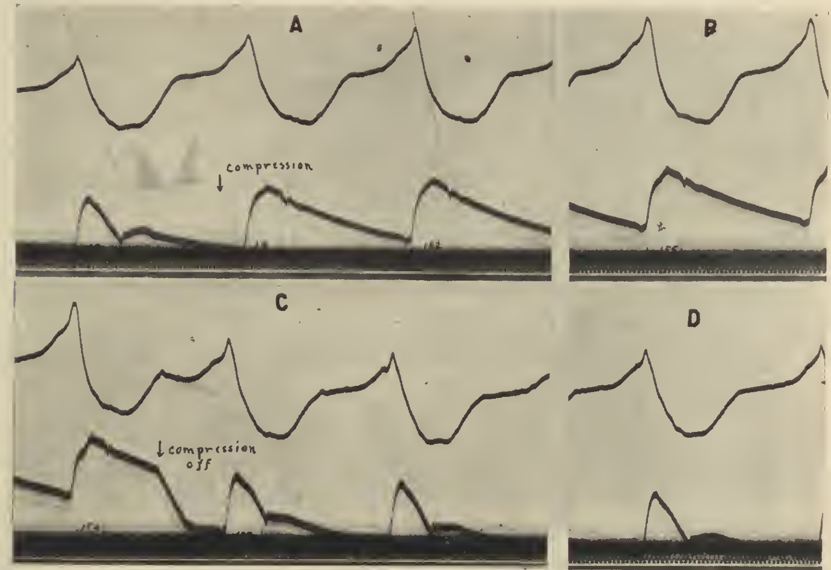

FIG. 37.—Four segments of ventricular volume and aortic pressure curves, illustrating detailed effects of aortic compression and decompression. *A*, immediate effect, systolic ejection steeper and of shorter duration; *B*, stabilized effect (tenth beat); *C*, immediate reversed effect of decompression; *D*, stabilized after-effects. (After Wiggers and Katz.)

tion, inasmuch as it could be reduplicated many times in each experiment. It occurred with remarkable promptness when compression was sudden, being evident during the first cycle following such compression (Fig. 37, *A*) and progressively decreased during the existence of compression, *B*. Upon decompression, *C*, the systolic ejection phase lengthened again.

The cause of the shortened systole is also indicated in this record. It is obvious that in such cases the shortening of systolic ejection is accomplished by a steeper ejection gradient, particularly in the earlier phase of ejection. In other words, the ventricles eject the same or

even a greater discharge in a shorter interval. This is the mechanism by which a good heart responds to increased resistance. When hearts are not capable of responding in this way the output is reduced, for when the phase of systolic ejection is reduced and the gradient of systolic ejection is not changed no other event can follow. Indeed, it seems that the *ability of the ventricles to respond to increased resistance with increased velocity of expulsion determines whether the systolic discharge is augmented, unaltered or decreased.* In the normal as well as in the hypodynamic heart the phase of systolic ejection is reduced. The former is able to respond (independent of venous pressure changes) by a greater velocity of ejection, so that the same or even a greater volume can be expelled in less time; the latter expels blood at the same velocity, with the result that the systolic discharge is decreased and diastolic dilatation becomes greater.

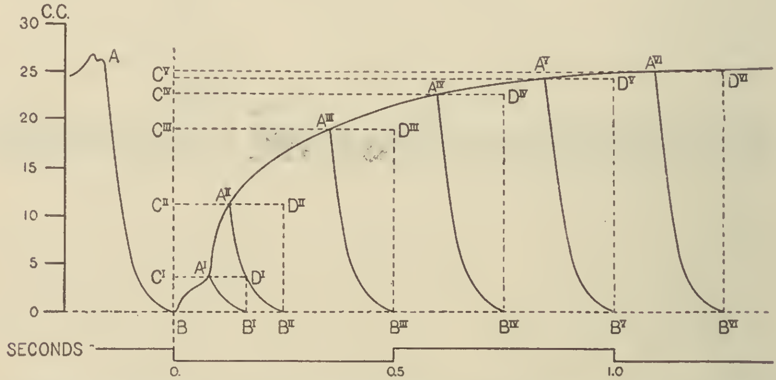

Fig. 38.—Scheme showing the volume curves at different lengths of cardiac cycles. (After Henderson.) A B, represents the maximal output during systole; B D^{VI}, the filling in a prolonged diastole. Arcs A^{I} B^{I}, A^{II}, B^{II}, etc., show amplitude of systolic stroke when systole begins at different periods of rapid inflow or diastasis.

The Influence of Changes in Heart Rate.—The fundamental effects of heart rate changes on the systolic discharge were first clearly analyzed by Henderson and are diagrammatically illustrated in Fig. 38. As the greatest degree of filling occurs early in diastole and comparatively little filling takes place during diastasis, it follows that as long as the heart rate is such that a diastasis phase exists the systolic ejection remains practically the same. Thus, the strokes A^{VI} B^{VI} and A^{V} B^{V} are practically equal and the stroke A^{IV} B^{IV} is only slightly smaller. As the cycle shortens, however, so that systole begins before the phase of rapid inflow is completed, the systolic discharge is reduced as in strokes A^{III} B^{III} and A^{II} B^{II}. The effect of this is that at rates up to 60 per minute the minute output increases in direct proportion to the heart rate; in fact, it is almost proportional up to 80 per minute. At 120 per minute (cycle, 0.5 second) the systolic discharge is reduced

to such an extent that the minute output, although still increasing, is no longer proportional to the rate. Between rates of 120 and 240 the minute output practically remains stationary; at still higher rates it progressively decreases. This tendency of the systolic discharge to decrease is unquestionably one of the safety mechanisms whereby the ejection of an excessive volume of blood per minute is prevented.

Such fundamental mechanisms operate only, however, when the rate of filling and rate of discharge remain constant, *i. e.*, when the smaller curves recorded at rapid rates can be superimposed on the larger beats at slower rates. If, however, the gradient of either the ejection or the filling curve should alter as the heart rate changes, such simple relations would no longer hold. Henderson and his collaborators maintain that the curves at different heart rates must remain superimposable under normal conditions of the circulation, and have consequently formulated their *law of uniformity of cardiac behavior,* according to which the systolic discharge can only vary as a result of heart rate changes. As previously indicated, recent work has shown that the gradient of the systolic as well as the diastolic curve may alter under conditions which increase either the venous pressure or arterial resistance. It is pertinent, therefore, to inquire *whether, under conditions of normal heart rate variation, the ejection curves can also alter their contour.* Changes in heart rate are normally the result of: (*a*) Variable vagus action; (*b*) variable action of accelerator nerves; (*c*) chemical influences, and (*d*) temperature changes.

Vagus Changes.—Detailed analysis of volume curves have shown that the contour of the volume curves alters appreciably during the course of vagal stimulation (Fig. 39). In the first vagal beat we observe a very pronounced amplitude and an increase in systolic ejection; in successive beats the gradient becomes less and less steep and finally the lower segment corresponds fairly well with normal beats. The effect of this is that the systolic phase is progressively lengthened as stimulation continues, an observation that has also been found by the author in intact animals. These changes are due to the variations in diastolic filling and the resulting initial volumes and tension. In the first beat auricular systole is particularly vigorous and, in the presence of increasing venous pressure, adds a large increment to ventricular filling. As stimulation continues the amplitude of auricular contraction is progressively reduced, however (Wiggers), and finally little is added to ventricular filling (Fig. 39, *B C D*). This is one factor. Another is the changing rate of early diastolic inflow. Comparison of curves *A* and *B* shows that the rate of inflow appears at first to be reduced and later increased. The temporary reduction is really due to the fact that at more rapid rates venous pressure and auricular systole combine to fill the ventricle early in diastole, whereas at slower rates the effect of auricular systole occurs separately. The

subsequent increase in early diastolic inflow is attributed to the increasing venous pressure as a result of long diastole. When such curves are superimposed as in the upper series of Fig. 40 it is apparent that while under stabilized conditions the beats are approximately superimposable (*e. g.*, *N* and *S*), they are far from being so when temporary heart rate variations occur as a result of vagal influence.

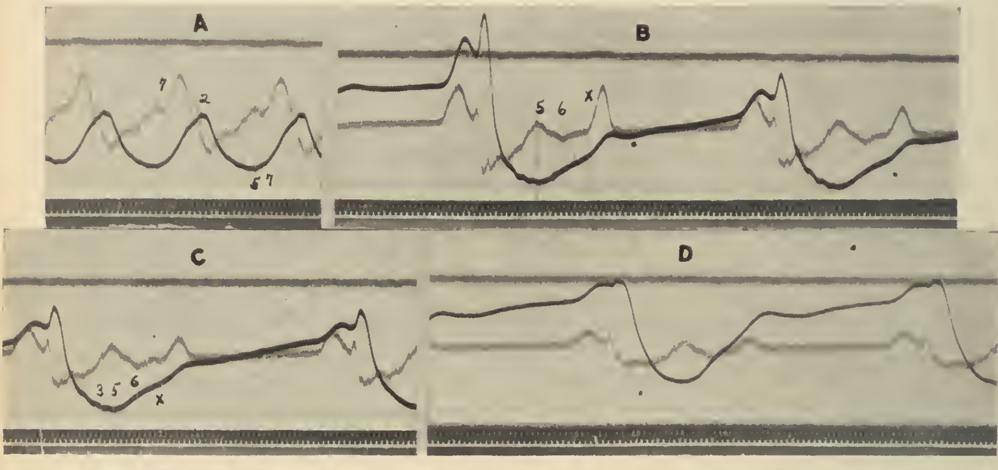

FIG. 39.—Four segments of optical volume curves and left auricular pressure curves, showing effect of brief vagal stimulation. *A*, normal beats; *B*, first and second vagus beats; *C*, fourth and fifth beats; *D*, stabilized beats. Observe changes in contour in various beats and diminishing vigor of auricular contractions. Note effects of isolated auricular contractions at *X*. (After Wiggers and Katz.)

The Effect of Accelerator Stimulation.—The effect of accelerator nerve stimulation on the volume curves has been investigated by Henderson and Barringer, who believe that deviations from the normal contour occur only when the heart is below normal in vigor. Katz and the author, however, could not explain the very extraordinary changes in length of systole, except on the basis of alteration in the contour of the volume curves. Subsequently, we also demonstrated marked changes when the accelerator mechanism is stimulated by epinephrin. The ejection gradient becomes much steeper, the phase of systolic ejection much shorter, rapid diastolic inflow much more rapid and auricular systole more vigorous. As shown in beats *D* and *E* of experiment C 292, *IX* in Fig. 40, it is quite possible, by virtue of such effects, for the heart to eject volumes that are larger than normal and equivalent to slow vagal beats, even though the rate is greatly accelerated.

We are, therefore, forced to the conclusion that *even under quite normal conditions changes in heart rate are not the only factor which necessarily dominates the volume of ventricular discharge.*

The Influence of the Inherent Cardiac Condition.—The fact that volume curves at different heart rates are not superimposable is only in part explainable as due to concomitant changes in venous and arterial pressures and their effect on initial volume and initial tension. In a measure, they must be referred to direct or indirect effects which improve the inherent contractile function of the heart in other ways than through changes of initial volume (Wiggers and Katz). That, on the other hand, the contractile function may also be depressed is

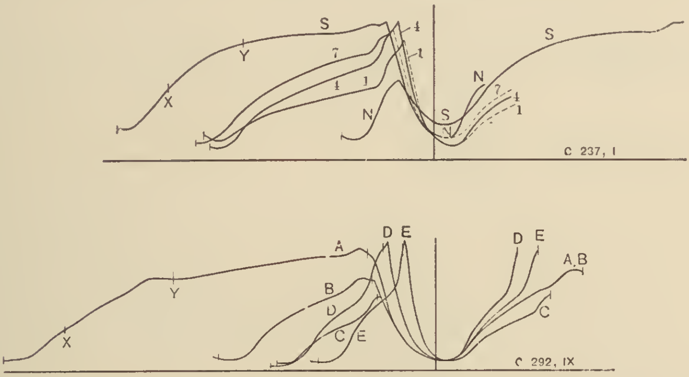

Fig. 40.—Two sets of transcribed curves, showing lack of superimposability at different heart rates (one-third actual size).

C 287. Series of vagus beats showing immediate and stabilized effects on volume curves, *N*, normal. 1, 4 and 7 represent first, fourth and seventh vagus beats. *S*, stabilized vagus beats. Curves matched at end of systole. Note: Failure of superimposability in all vagus beats with normal and each other; progressive lengthening of systolic ejection, due to more gradual gradient; progressively diminishing auricular contribution; increasing inflow during early diastole and diastasis, due to augmenting venous pressures.

C 292, *IX*. Series of beats at different heart rates. *A*, *B*, stabilized vagus beats with different diastolic lengths. *C*, normal; *D*, early epinephrin action, producing slight acceleration; *E*, after-effect of epinephrin. Note: Failure of epinephrin curves to superimpose even approximately on stabilized vagus and normal beats as regards systolic or diastolic portions, also extreme abbreviation of systolic ejection phase with steeper systolic strokes. Note: Only approximate superimposability of normal curves, *C*, with stabilized vagus curves, *B* and *A*. Note increased auricular contribution during epinephrin and decreased contribution of stabilized vagus as compared with normal, *C*.

well demonstrated during the course of laboratory experiments and evident in pathological conditions of the heart muscle (*cf.* page 561). Whether such influences also operate in the body under conditions that may be classified as normal cannot at present be stated. As the heart muscle suffers from long experimental procedures when it is submitted for a long time to strain or affected by depressing drugs, such as chloral, chloroform, etc., a time arrives when, in spite of increasing venous pressure, the systolic discharge is reduced and a dilatation of the heart takes place. Coincident with such changes,

the initial intraventricular pressure increases but the pressure elevation during systole becomes reduced. The writer has designated this as a *hypodynamic condition* in which it is inferred that the contractile function is at fault. Such results have, however, also been attributed to a loss of *tonus*. This is, of course, permissible provided we choose to define tonus with Patterson, Piper and Starling as "synonymous with the physiological condition or fitness of a muscle and its measure the energy set free per unit length of fiber." To the physiologist the term "tonus" has come to signify a sort of a sustained partial contraction of muscle tissue by virtue of which the muscle fibers resist stretching more than they would by virtue of the inherent elasticity alone. According to this conception, the ventricular tonus varies

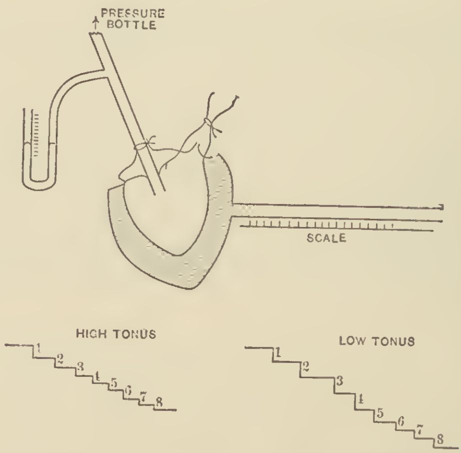

Fig. 41.—Diagram illustrating principle of measuring volume-elasticity coefficient of relaxed ventricle. The lower curves illustrate distention curves in hearts with high and low tonus, each step representing an equal increment of intraventricular pressure.

directly as the volume-elasticity coefficient of the relaxed heart, *i. e.*, the ratio of the pressure increase to the volume increase, $\frac{\triangle p}{\triangle v}$.

This relation may be studied after the fashion schematically illustrated in Fig. 41. Let us suppose that in such a preparation sufficient fluid is admitted into the ventricle to raise the intraventricular pressure by eight equal increments. The volume changes corresponding to each of, say eight, such pressure elevations may then be plotted in step-like fashion. Comparison of curves from ventricles under varying conditions of tonus make it quite obvious that when tonus is low a much greater increase in volume accompanies a given pressure increase than when tonus is high; or, stated in the reverse, the same

volume change is associated with a much greater pressure change when tonus is high than when it is low. If we adhere to this the more current conception of tonus, we are not warranted in referring the hypodynamic effects above discussed to tonus changes unless an abnormal relation between $\frac{\triangle p}{\triangle v}$ is demonstrated (*cf.* also page 563).

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CHAPTER V.

THE MECHANICAL ENERGY OF THE HEART BEAT.

BLOOD-PRESSURE AND BLOOD FLOW.

As soon as intraventricular exceeds arterial pressure and the semilunar valves open, a certain quantity of blood, designated as the *pulse volume*, is suddenly ejected into the aorta, due to the difference of pressure developed in the ventricle and that present in the arteries. Since the arteries are already distended at the time of this systolic discharge, room must be made either by moving the column of blood onward or by increasing the capacity of the arterial system. In the former case the pressure energy generated by the heart is transformed to kinetic energy, or energy of flow; in the latter case it is stored as potential energy by further distending the arterial walls. Normally, less than 1 per cent of the total pressure energy is immediately converted into flow, but the actual ratio of flow to pressure energy is determined by the distensibility of the arterial walls and the volume of systolic discharge. The distensibility of the arterial wall is inversely proportional to the volume-elasticity coefficient of the entire arterial system, *i. e.*, the ratio of the pressure increase to the volume increase. This coefficient varies: (1) With the diastolic pressure in the artery; (2) with the degree of tonus; and (3) with the physical characteristics of the arterial wall. Thus, an arteriosclerotic artery has a higher coefficient of elasticity than a normal artery (*cf.* MacWilliam). The greater the coefficient becomes the less fluid will be accommodated, and hence a greater conversion of potential energy into kinetic energy takes place. As regards the influence of systolic discharge, Evans and Matsuoka found that, using the mean velocity of blood flow in calculation, the velocity factor might increase from 0.029 per cent of total energy under low discharge to 6 per cent of the total work when discharge is great. Subsequent recalculations indicate, however, that the magnitude of change is even greater than this. Thus, if the velocity during systolic ejection is used in calculation, the velocity factor may amount to as much as 9 per cent of the total work (Evans).

The potential energy stored by the distended walls during systole as pressure is reconverted into kinetic energy during diastole when blood ceases to be injected into the aorta, thus ensuring practically a constant flow through the smaller vessels during diastole as well as systole. Hence, the arterial pressure reaches its maximum in systole and its minimum during diastole. These pressures have been termed *systolic* and *diastolic pressures* respectively. Their difference is called the *pulse pressure* (Figs. 42 and 43).

According to Fleisch, not all the energy used in distending the arteries is restored without loss as kinetic energy of flow during diastolic relaxation. The loss thus incurred is the greater the more the arteries are distended initially, and is larger in the more peripheral than in the central vessels. We may suppose that this is due to a partial conversion of the mechanical energy into heat.

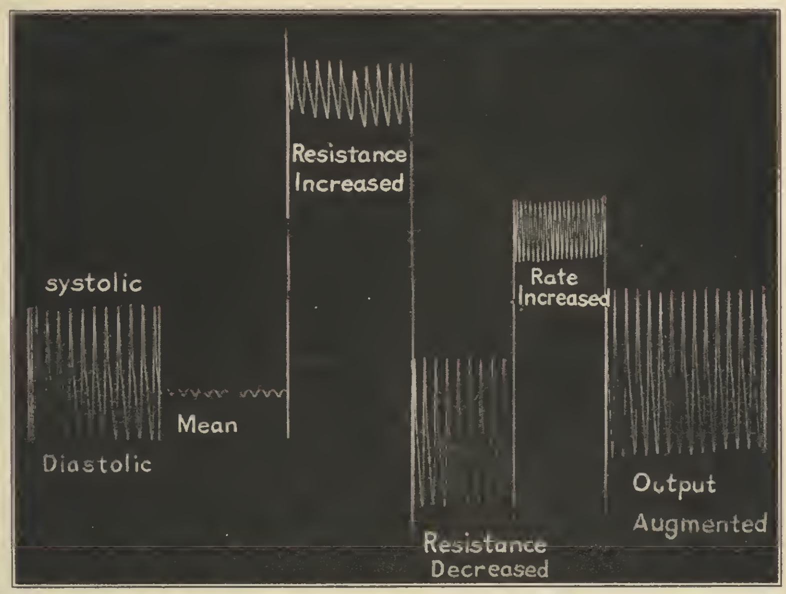

FIG. 42.—Arterial pressure variations taken from an artificial circulation machine under different conditions described in text.

Factors Modifying Blood-pressure.—The fundamental factors determining the actual and relative heights of these pressures under different conditions may be conveniently studied by some form of artificial circulation machine. This not only has the advantage that the factors can be adequately varied and controlled, but the pressure changes occur slowly enough to enable an ordinary mercury manometer to follow them fairly accurately, which it cannot do in animal experiments.

When the pressure variations in the tubes representing the arteries are thus recorded (Fig. 42) the pressure rises during systole and falls during diastole. If *the peripheral resistance* is now increased both systolic and diastolic pressures progressively increase, the diastolic pressure rising more than the systolic, however. This continues until a stable equilibrium results, as shown in Fig. 42, where the pulse pressure continues much reduced.

The cause of these changes is readily understood if we bear in mind that the pressure changes are largely controlled by the volume of

blood leaving the arterial system during systole and diastole as compared to the volume injected by the heart during systole. Let us suppose that normally each systole ejects 60 cc, of which 15 cc leave the arterial system during systole and 45 cc during diastole. As the peripheral resistance is suddenly increased the peripheral outflow is reduced in the next few beats, say to 51, 53, 55 and 58 cc respectively. Obviously there is always a remainder at the end of each cycle which must be accommodated by distending the aorta and its branches. This causes a progressive increase of pressure until a time comes when the peripheral outflow again equals systolic discharge and a new but stable pressure equilibrium is established. When this happens the distensibility of the arterial tubes for equal pressure increments is diminished; consequently, the ejected volume is less readily accommodated during systole and a larger share of the total energy of ventricular ejection must be converted into flow. Thus, we may suppose that instead of 15 cc now 25 cc leave the arterial system during systole. Assuming that the total energy of systolic ejection is a constant, then such a greater velocity energy can only be acquired at the expense of potential energy of pressure and the systolic pressure is elevated proportionately less. This increased systolic outflow from the arterial system has the effect of reducing the peripheral outflow in diastole from 45 to 35 cc. The inevitable result of this is that a relatively larger remainder of the total available diastolic energy is left over and acts to elevate diastolic pressure proportionately more.

At a constant peripheral resistance and constant volume of ejection a *sudden increase in heart rate* leads to a similar progressive increase in systolic and diastolic pressures, the diastolic pressure again rising more than the systolic and the pulse pressure decreasing. This continues until a stable equilibrium is reached. Obviously the increase of the general pressure level is again due to the fact that the systolic discharge exceeds the peripheral outflow during each heart cycle. In this case, however, the peripheral outflow is reduced by virtue of the curtailment of the period of diastole. Nevertheless, at the end of diastole an extra volume of blood must be accommodated by distending the elastic vessels and raising the arterial pressures. An equilibrium is reached when the progressive distention of the arterial walls has elevated arterial pressure so far that blood is moved on more readily than it is accommodated during systole. Thus, we may find that again 25 cc leave the arterial system during systole and 35 cc during diastole, with the consequent result before analyzed that systolic pressure rises proportionally less than diastolic and the pulse pressure decreases.

If at a constant heart rate and with unvarying peripheral resistance the *systolic discharge increases* a different relation of systolic and diastolic pressures obtains. Both pressures progressively increase, but systolic pressure now increases more than diastolic, a relation that holds after stabilized conditions have been established (Fig. 42). During the

period of pressure elevation the systolic discharge again exceeds the peripheral outflow. Thus, we may suppose that when the systolic discharge increases from 60 to 70 cc the peripheral outflow during the next few cardiac cycles averages 63, 66 and 69 cc. The remainder at the end of consecutive diastoles serve to elevate the pressures. Under this condition, and contrary to the effects previously described, the progressively greater volume of peripheral outflow occurs chiefly during diastole, for both the peripheral resistance and the duration of diastole are unaffected. Thus, under stabilized conditions, when peripheral flow and systolic discharge are again equal, we may suppose that the systolic outflow has increased only from 15 to 18 cc, while the diastolic outflow is augmented from 45 to 52 cc. With the systolic outflow so little affected, the larger share of energy of the more vigorous discharge must be stored as potential energy during systole and accounts for the relatively great elevation of systolic pressure. The relatively large outflow during diastole, on the other hand, must be accompanied by a proportionally great fall of pressure and accounts for the relatively low diastolic pressure. It may be further added that, owing to this great diastolic outflow and relatively low diastolic pressure the distensibility of the arteries is not greatly affected and, therefore, the extra volume ejected by augmented systole is largely accommodated in the large vessels. It is obvious, however, that to this there is a limit. If arterial pressures are already high (*e. g.*, owing to a high resistance or when the elasticity of the arterial wall is impaired), then the reduced distensibility of the arterial wall comes into play. In such cases it may prove easier to move the blood column onward than to further distend the vessels. Under such conditions the systolic peripheral flow may augment so much that the systolic pressure rises relatively less than diastolic and the pulse pressure decreases. This, however, must be regarded as an abnormal and not a normal consequence.

The effects of the above-mentioned factors on the systolic, diastolic and pulse pressures, and the significance of changes in pulse pressure, are summarized in the following table:

I. Factors Affecting Blood-pressures.

	Systolic pressure.	Diastolic pressure.	Pulse pressure.
Increased peripheral resistance	+	++	−
Decreased peripheral resistance	−	−−	+
Increased heart rate	+	++	−
Decreased heart rate	−	−−	+
Increased systolic discharge	++	+	+
Decreased systolic discharge	−−	−	−

II. Significance of Increased Pulse Pressure.

Decreased resistance	Decreased systolic and diastolic pressures	Heart rate same.
Decreased rate	Decreased systolic and diastolic pressures	Heart rate slower.
Increased output	Increased systolic and diastolic pressures	Heart rate same.

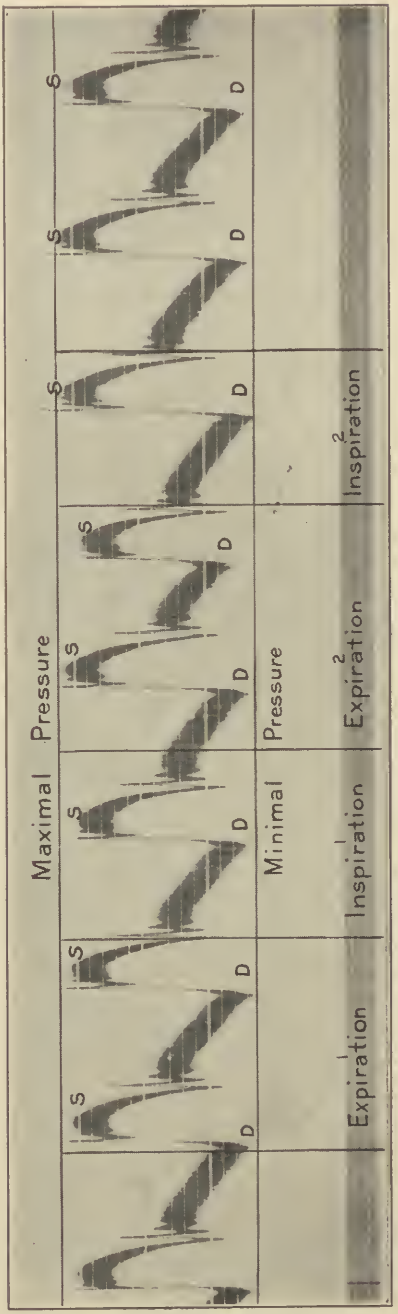

FIG. 43.—Variations of systolic and diastolic pressures in subclavian artery of dog. The distinction between maximal and minimal pressure is shown. During first expiration and inspiration, variations are due to mechanical influence of respiration; during second expiration and inspiration they are controlled by predominant effect of heart-cycle changes. *S*, systolic; *D*, diastolic pressure.

Conceptions and Relations of Systolic and Diastolic Pressures.—The pressure within the arteries of an animal and in man do not vary in so simple a fashion as is indicated by artificial circulation apparatus, hence it is desirable to establish precise conceptions of circulatory changes.

In the first place, the pressure does not increase throughout systole but falls during the latter phase. Furthermore, in the central vessels the systolic top is represented by a peak and a summit, the former sharp (primary oscillation), the latter more rounded and corresponding to the true systolic level of pressure in the ventricle. When resistance is fairly high the summit constitutes the highest point both in animals and in man (Figs. 22 and 23). It not infrequently happens, however, that the preliminary peak is the highest point (Fig. 43). Inasmuch as the summit corresponds to the actual systolic pressure within the ventricle, it would seem desirable to limit the term *systolic pressure* to the highest point on the summit. The term *diastolic pressure* may likewise be accurately limited to the pressure reached in diastole before the preliminary oscillations occur.

In the second place, the systolic and diastolic pressures of consecutive beats fluctuate with the phases of respiration and change with the duration of consecutive cycles (Fig. 43). It is apparent that systolic and diastolic pressures are not equivalent to the *maximum* and *minimum pressures* reached, nor is the *pulse pressure* equal to the *maximal-minimal pressure difference* recorded by valved mercury manometers.

That this distinction between systolic and maximal pressures, on the one hand, and diastolic and minimal pressures, on the other, is of more than academic interest is shown by the fact that in dogs the systolic pressure varies from 7 to 28 mm. during the act of respiration while the diastolic pressure varies from 2 to 30 mm. The *average pulse pressure* of consecutive beats equaled from 66 to 98 per cent of the maximal-minimal pressure difference (Wiggers, Eberly and Wenner). Although impossible to determine quantitatively, it is probable, from continuous human blood-pressure tracings (Erlanger and Festerling, Wiggers, Snyder), that these differences are great enough in man to warrant a distinction.

The Pressor Influence of Respiratory Movements.—If respiration ceases for a time, both systolic and diastolic pressures fall until a new pressure level is reached. It is possible to estimate the "*pressor effect*" of respiratory movements by taking an average of the systolic and diastolic variations and comparing these with the pressure during apnea temporarily induced by stimulating the central vagus for twenty to thirty seconds with a weak current. Under such conditions vasomotor reactions are delayed long enough in the dog so that the mechanical effect of respiration can be determined. The following data in

which the figures represent millimeters of mercury illustrate the method:

Average systolic pressure.	Average diastolic pressure.	
91.3	44.3	During natural respiration.
88.4	38.9	During apnea.
2.9	5.4	

In this case the normal act of respiration elevated the average systolic pressure 2.9 mm., or 3.1 per cent, while it increased the diastolic pressure 5.4 mm., or 8.4 per cent. In dogs this *respiratory pressor factor,* as the percentile figure may be termed, is responsible for 2 to 3 per cent of the average systolic and 3 to 4 per cent of the diastolic variation. Its importance consists not only in the small share it plays in thus maintaining normal blood-pressure, but also in the fact that when arterial pressure is low, deep respirations contribute a relatively larger share to blood-pressure variations (Wiggers, Eberly and Wenner).

Rhythmic variations of the cardiac cycle, such as occur normally due to a rhythmic activity of the vagus center or such as occur in abnormal rhythms of the heart (page 365), also modify the blood-pressures. We might anticipate from the hemodynamics evolved from an artificial circulation apparatus that a shortened cycle (*i. e.,* an increased rate) would elevate both systolic and diastolic pressures, while lengthened cycles would depress them. Actual records with optically recording manometers (Fig. 43) show that, when fleeting variations in the cardiac cycle are concerned, *a shortened cycle* (fifth wave, Fig. 43) *is followed by a decreased systolic and increased diastolic pressure.* A lengthened cycle (*cf.* sixth wave, Fig. 43), on the other hand, causes an elevation of systolic pressure, owing to the increased systolic discharge and a fall of diastolic pressure in the succeeding wave, owing to the long diastolic pause. In other words, changes in cycle length are always accompanied by changes in systolic discharge, and the effects on arterial pressures are determined by the resultant of these two variables.

The variations of systolic pressure deviate from this rule only when the alteration of the cardiac cycle does not change the filling (*i. e.,* in very slow hearts) and when a change in rate lasts for a considerable period, so as to allow the pressure to become stable at a new level (Wiggers).

In the large arteries the pressures vary little from those in the aorta. It is not until the smaller arteries are reached—such, for example, as enter into the formation of the circle of Willis—that the mean pressure is conspicuously decreased (Poiseuille). The minimal pressure is also constant in the larger arteries, but the maximal pressure declines somewhat in arteries of such caliber as the thyroids (Hürthle, Dawson).

Relative Pressures at Different Points of the Vascular System.—As we pass to the smaller arteries, both maximal and minimal pressures diminish—the former more than the latter. This reduction continues until, in the smaller arteries, a constant pressure exists during systole and diastole.

Considerable theoretical discussion has arisen as to the point of the vascular system where the arterial pressures fall most steeply. Following Poiseuille, it is generally believed that the greatest drop occurs between the arterioles and capillaries (for literature *cf.* Schleier). Other investigators, however, have contended that the greatest fall occurs in the small arterioles (Campbell, Levy, etc.; for literature see Danzer and Hooker). The most accurate idea of the actual pressures in the arterioles, capillaries and veins has been obtained by directly examining the vascular loops of the skin under a microscope. To do this a drop of glycerin or oil is placed on the epidermis, which is then illuminated by a strong light. Intravascular pressure is determined by applying pressure to the skin by means of a microtonometer and observing the amount required to obliterate or stop the flow in any particular vessel or group of vessels under observation (Lombard, Danzer and Hooker, Basler). (For details *cf.* page 389.)

The following values, expressed in millimeters of mercury, were obtained by Lombard:

Most resisting capillaries and arterioles	60–70
Average capillaries	35–45
Most compressible capillaries	15–25
Most superficial veins	15–20
Subpapillary venous plexus	10–15

Danzer and Hooker found capillary pressure variations in thirty-one individuals from 17.5 to 26.5 mm., an average of 22.2 mm. Hg. Using a similar method, Basler obtained somewhat lower figures for capillary pressures in man, viz., 12 to 18 cm. water. Hill, who uses as a criteria of capillary pressure not the moment when capillary flow is entirely stopped but the point where the flow just begins to lessen, reports his values as low as 10 to 12 cm. of water.

Apparently there is a fall of blood-pressure in the passage from the small arteries through the capillaries to the veins of some 40 to 50 mm. mercury, which indicates that a great resistance is encountered in the capillary field. It may be noted in passing that the capillaries are not the only fields where resistance is offered, for if we accept 90 mm. as a mean aortic pressure in man the fall from the aorta to the arterioles examined by Lombard is nearly as great, showing that the arterioles themselves offer considerable resistance to the flow of blood.

The venous pressure, as a whole, is lower than that in the capillaries and decreases as the central veins are approached; indeed, owing to the negative intrathoracic pressure on the exterior of the intrathoracic

veins, it actually becomes negative as regards atmospheric pressure. Thus, figures given by Burton-Opitz from the dog show the following progressive decrease: Renal vein, 10.9 mm.; saphenous vein, 7.4 mm.; femoral vein, 5.4 mm.; brachial vein, 3.9 mm.; external jugular vein, 0.5 mm.; superior vena cava, −1.4 to −2.9 mm. Hg. (For a consideration of arterial and venous pressures in man *cf.* Chapter XVII.)

The Velocity of the Blood Flow.—By the velocity of flow is meant the rate at which a certain cross-section of the blood column passes a definite point and is determined by the difference in pressure between two places at any time.

Methods.—The average velocity in any vessel may be calculated from the volume flow per minute, according to the formula $L = \frac{V}{\pi r^2}$, in which L equals the length of the blood column passing per unit time, and hence represents the velocity; V equals the volume flow per unit time determined by a stromuhr, and r, the radius of the artery. This, however, gives only the mean velocity and not the variations occurring during systole and diastole. To establish these variations the hemodromograph was devised by Chauveau. This instrument, described in most text-books of physiology, has proven of little real value. In the first place, its use is restricted to large animals, the horse being apparently the only animal in which it has been used. Secondly, coagulation interferes with its prolonged use in any experiment. Lastly, the movable mass of the apparatus is so great that it is not capable of following rapid changes of velocity accurately.

Still another method of studying variations in velocity employs the principles of Pitot's tubes. The principle of their use is as follows: If into a tube in which fluid under pressure is flowing, two tubes are introduced in such a way that the opening of one is directed against and the other with the stream, a difference of pressure in the two tubes takes place which at any time is proportional to the velocity. This principle was applied by Cybulski to study variations in the velocity of the blood stream, but the heavy mass of the mercurial column of his manometer rendered it incapable of accurately following the pressure changes. The same principle has been practically applied in the laboratory of Frank (Fig. 44). He inserts a double-barreled cannula, with lateral openings pointing in opposite directions, into a side branch of the vessels in which the velocity is to be measured. This is connected with a double chamber the cavities of which are separated by a rubber membrane and filled with fluid. In a recent form of apparatus, Frank has sought to record the movements of this differential membrane by cementing a small mirror to it and reflecting a beam of light through the glass side of the chamber. To prevent the upward diffusion of blood and thus the interference with the passage of the light beam, he interposes a delicate membrane between

the outer chamber and the artery. The principle of this apparatus is shown in Fig. 44.

The velocity flow in man was at first deduced from the volume curve of an arm enclosed within a plethysmograph, recorded by some form of volume recorder (Fick). The idea upon which this was founded assumes that the venous outflow is constant. The first differential quotient of the volume curve is then proportional to the velocity. Garten has improved upon this method by substituting a soap-bubble as a registering mechanism. Hewlett and Van Zwaluwenburg recorded volume pulses with an optical capsule while the venous outflow was temporarily occluded, and from these curves plotted the velocity curves (*cf.* Fig. 45).

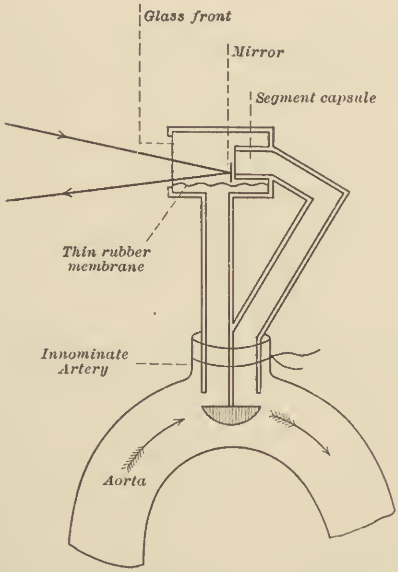

FIG. 44.—Diagram showing the principle of Frank's differential manometer for recording variations in velocity.

To obviate the necessity of determining a whole series of tangents from the volume curve, v. Kries devised the *tachograph* to record the velocity. This apparatus, in which the variations of a gas flame were photographed, had obvious disadvantages. It has been adapted and improved by Frank in the following manner: The arm is placed in an arm plethysmograph connected with a segment capsule. The plethysmograph, instead of being kept closed, communicates with the outside air by a second opening. The capsule, therefore, records not the volume change but its differential quotient, "the velocity change" directly. It is important to keep the chamber as small as possible

and the external communication as large as is permitted by the sensitiveness of the recording mechanism. This appliance records the velocity changes accurately only when the variations are not too extreme and rapid. If this is the case the records may become mixtures of volume curves and *tachograms*, as the records of velocity are called.

Several attempts have been made to record tachograms of the central arteries. This is accomplished, though only imperfectly, by pressing a receiver into the supraclavicular fossa and connecting this with a registering flame (Müller and associates). Similar curves have been recorded from these areas by Hill with the so-called hot-wire sphygmograph (*cf.* page 198). It is probable, however, as v. Kries points out, that such tracings are not true velocity curves but represent differential pressure curves.

Velocity Determinations.—According to Poiseuille's law the mean velocity of a stream is directly proportional to the cross-sectional area of the tube and the pressure gradient. Consequently, the product of these two multiplied by a coefficient depending on the viscosity and physical nature of the fluid determines the mean velocity. Many facts indicate, however, that it is not possible actually to calculate the velocity of the blood stream in this way, not so much because it is a complicated system of dividing tubes but chiefly because the cross-section area varies under a variety of conditions. Direct stromuhr experiments indicate, however, that in dogs the mean velocity is somewhere between 240 and 260 mm. per second in arteries like the carotid (Vierordt, Tschuewsky). The average velocity decreases as the smaller vessels are approached. In the capillaries the rate of flow is often less than 1 mm. per second. Thus, Hürthle reports a velocity of 1.7 mm. per second in mesenteric vessels and Basler obtained ranges from 0.24 to 1.7 mm. per second. In the peripheral veins it is more constant and increases again as the central veins are approached. Thus, the flow in the jugular veins equals 147 mm. per second, while in the femoral it is 61.6 mm. per second and in the renal vein 63 mm. per second (Burton-Opitz). We may, therefore, picture the average velocity as gradually decreasing from the heart to the capillaries and increasing slowly again as the blood is returned to the heart. This is due to the fact that while the size of individual vessels decreases as the periphery is approached, the total stream bed widens and as blood is collected and returned to the heart it narrows again.

The changes in velocity which occur during each cardiac cycle have been less accurately established. Trustworthy velocity curves by the instrument devised by Frank have not as yet been reported. The figures given by the hemodromograph indicate that in the horse the flow may attain a maximum velocity of 520 mm. per second and fall to 150 mm. during diastole (Lorlet, quoted by Tigerstedt). These observations are, however, only approximate. Theoretical analysis of

the aortic pressure curves indicates, however, that in the aorta near the semilunar valves the velocity is very great during systole, but practically zero during diastole; in fact, during the earliest moment of the incisura there is probably a slight backward flow. Simultaneous optical registrations of pressure and volume changes in the blood stream of the carotid and femoral arteries during systole and diastole indicate that as we move away from the semilunar valves we obtain both a systolic and a diastolic flow (Hürthle). The flow accelerates markedly in systole but in the latter part diminishes rapidly, and this slower rate continues through diastole. Tachograms of the human forearm (Fick, v. Kries, Hewlett and Van Zwaluwenburg) indicate that the velocity of flow increases rapidly with the pulse wave and reaches a maximum almost midway on the ascending stroke of the arterial pulse. It then rapidly decreases again until at the time of the dicrotic wave a slight secondary acceleration occurs (Fig. 45).

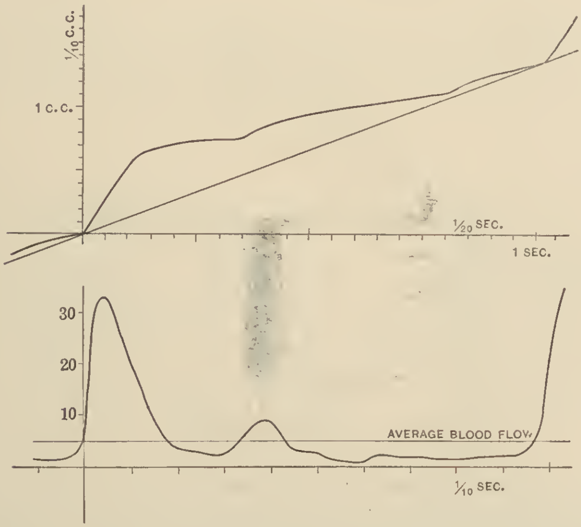

Fig. 45.—Upper curves, pulse-volume flow of arm; lower curve, reconstructed tachograms or velocity curves of arm. (After Hewlett and Van Zwaluwenburg.)

The Volume Flow of Blood.—By volume flow is meant the *volume* of blood passing through a vessel or organ in a definite time, independent of whether its velocity is great or small. The volume of blood passing through the aorta measures the total volume passing through all the organs with the exception of the heart walls. The volume flow per minute has been termed the *minute volume* and is equal to the product of the *pulse volume* (*i. e.*, the quantity flowing during one heart cycle) and the heart rate per minute.

The magnitude of the minute volume, and also of the pulse volume, has been determined in various ways in animals, namely:

1. By perfusing a heart in such a way that fluid passes in normal fashion into and through the cardiac chambers and measuring the outflow (Stolnikow, Howell and Donaldson, Patterson and Starling). Theoretically, the aortic outflow should be directly measured, but as this causes the heart to act without arterial resistance, the flow beyond an arterial resistance has been used (Patterson and Starling). This is obviously only an accurate estimate of the minute output when arterial pressures are stabilized (*cf.* page 124).

2. By inserting a stromuhr into the aorta after temporary interruption of the current (Tigerstedt).

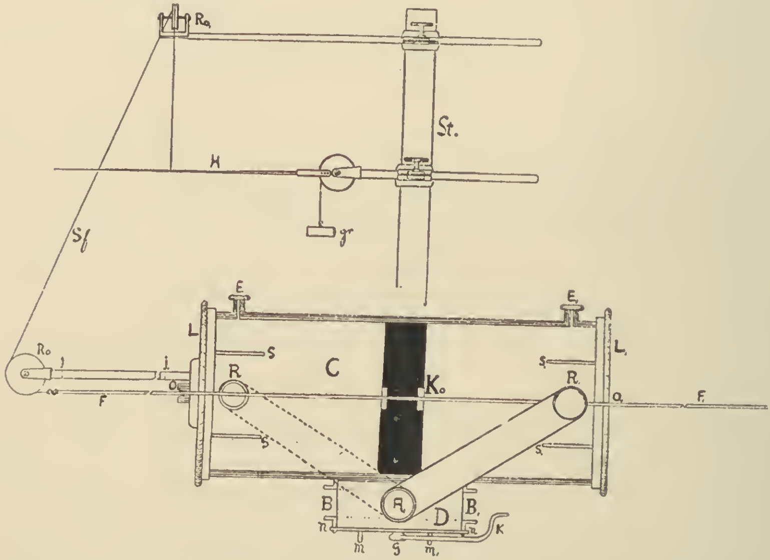

FIG. 46.—Recording stromuhr. Fluid entering the right compartment of cylinder (*C*) via *AR* pushes the plunger (*K*) to the left and causes a downward movement of the lever (*H*). On reversing the plate (*D*) by means of a handle (*k*) blood flows via *AR* into the left compartment and pushes the plunger to the right, thereby raising the lever (*H*). (After Burton-Opitz.)

Various forms of stromuhr have been devised and are described in current text-books of physiology.[1] Fig. 46 shows the principle of a graphically recording form, devised by Burton-Opitz, which has the advantage that hydrostatic variations are avoided by the employment of a horizontal barrel. An optically recording stromuhr has been described by Hürthle.

[1] For a description of various forms, *cf.* Tigerstedt's Handbuch der physiologischen Methodik, 1913, **2**, part iv, 105.

3. By the blood dilution method (Stewart): Salt solution[1] is allowed to slowly enter for a definite number of seconds into the left ventricle through a tube passed down the carotid. A sample of the mixture of blood and salt solution is collected from a femoral branch, where its arrival is detected by a change in electrical resistance. The quantity of blood with which the solution was mixed in the ventricle can be determined by adding to a sample of blood previously drawn the same saline solution until its conductivity is the same as that of the solution collected in the experiment.

4. By the gasometric method (*cf.* page 377).

5. By determining the cardiometric variations of the ventricle quantitatively and calculating the minute volume.

By one or many of these different methods the pulse volume and minute volumes have been determined in different animals, man included. As the systolic discharge and minute volume naturally vary with the size of the animals the results have been calculated on a basis of body weight, and by assuming a corresponding discharge in man, recalculations have been made for the systolic discharge in men of standard weight (70 kilos). The following table shows some of the results obtained on the lower animals:

Minute Volume per 100 Grams.

Barcroft and others (4) (goats)	5.50 to 22.00
Bock and Buchholtz (3) (dogs)	11.40 to 17.90
Gréhant and Quinquaud (4) (dogs)	8.40 to 14.50
Henderson (5) (dogs)	1.30 to 2.60 slow hearts 2.00 to 3.90 rapid hearts
Howell and Donaldson (1) (dogs)	19.70
Murlin and Greer (4) (dogs)	8.90 to 14.60
Rothberger (5) (cats)	1.80 to 14.00
Stewart (3) (dogs)	13.90 to 22.20
Stewart (recent reports) (3) (dogs)	8.90 to 23.40
Stolnikow (1) (dogs)	2.50 to 34.60
Tigerstedt (2) (rabbits)	7.56 to 8.44
Zuntz (4) (dogs)	9.00

Numerals in brackets refer to methods used and correspond to numbers used in text above.

A comparison of the results of minute volume per 100 grams indicates that calculations transferred without reserve to a man weighing 72 kilos must give extraordinary variations, and that such comparisons are not without suspicions. This is, in part, due to the methods employed; in part, to the fact that normal conditions probably did not obtain during experimental conditions. Furthermore, the heart rates and periods of ejection do not correspond to those obtained in man, and finally the blood supply of normal tissue, like the metabolism

[1] Instead of salt solution, other harmless substances, which can be quantitatively determined, have also been employed, *e. g.*, sodium sulphocyanide (Henriques), NaI (Bock and Buchholtz).

rate, is not proportional to body weight but rather to surface area. Nevertheless, calculations made from the most reliable of these results indicate that the systolic discharge in man is not less than 50 to 60 cc and may be greater than 100 cc. The former figures conform to the earlier observations by gasometric methods (*cf.* page 383), but later results appear to conform more nearly to the latter figures. Thus, Douglas and Haldane give 110 to 114 cc and Henderson 132 cc as normal values for the systolic discharge. Using an entirely different method, Meek and Eyster have recently obtained figures ranging from 73 to 79 cc. (For details and literature *cf.* Chapter XVIII.)

The Work of the Heart.—The mechanical energy of the ventricular contraction is largely utilized in ejecting blood against an arterial resistance (*potential energy factor*), but to some extent also in imparting velocity to the arterial stream (*velocity* factor). The mechanical work may, therefore, be approximately calculated according to the sum of these two factors or $W = Q\,R + \frac{w\,V_2}{2g}$. In this formula W is the work; w, the weight of the volume ejected; Q, the quantity ejected; R, the mean arterial resistance in meters of blood (arterial pressure $\times$ 0.13); V, the mean velocity at the root of the aorta, and g, acceleration due to gravity (= 9.8).

Since blood is not ejected against a constant mean pressure but against a variable pressure, such calculations are not correct within 10 to 20 per cent (Frank) as regards the potential energy factor ($Q\,R$). Frank has shown, however, that when the changes in volume of ejection and the pressure curves are synchronously recorded in an accurate manner the potential energy factor of cardiac work may be accurately calculated by the following formula:

$$A = \int_{t_0}^{t_1}$$

where A is the work, P the pressure and V the volume considered at shortest consecutive intervals during the course of ejection, beginning with the opening of the semilunar valves t_0 and ending with their closure, t_1.

As regards the velocity factor, $\frac{w\,V^2}{2g}$, Evans has shown that while it is normally less than 1 per cent of the total energy of the ventricular contraction, it increases tremendously when the systolic discharge and velocity are augmented. Using the ordinary formula, Evans found that the velocity factor actually equals 20 per cent. Such conditions do not actually obtain, for with increased discharge the duration of systole alters. When with increasing venous return systole is lengthened, recalculation of the velocity factor by the formula $\frac{w\,(V\,C)^2}{g\,E^2}$ shows

that it is increased only to 9.5 per cent of the total energy. Evans submits the following complete formula, therefore, for calculation of the work of the heart:

$$W = 7\frac{Q\,R}{6} + \frac{w\,(V\,C)^2}{g\,E^2},$$

where C is the duration of the cardiac cycle and E the period of systolic ejection.

As the capacity of the ventricle for work is a function of volume and pressure as well as time, it is possible, when both pressure and volume curves are accurately recorded at the same time, to plot these relations as a surface area diagram or *work-diagram* (Frank). Frank has indeed devised an ingenious *work-indicator*, by means of which such a diagram can be directly recorded in the case of the frog's ventricle. In this apparatus, pressure and volume curves of the ventricles are simultaneously recorded. The registration is so adjusted that a beam of light is first projected upon a mirror pivoting on a horizontal axis of the volume recorder. Before striking the photographic plate it is reflected to a mirror of the pressure-recording system which rotates in a vertical axis. On being reflected upon this mirror the light beam encircles an area the surface of which is proportional to the work.

Owing to the fact that the volume curves of the mammalian ventricles cannot be separately recorded,[1] it has not proven feasible to apply this apparatus to the mammalian heart; indeed, it has not seemed desirable to attempt the construction of work-diagrams. Straub, however, has plotted such diagrams, which if they are not quite precise are, nevertheless, instructive. Their nature and method of construction are shown in Fig. 47): *I* represents the intraventricular pressure curve, in which the coördinates are pressure and time. *II* represents the volume curves similarly plotted on coördinates at right angles. By projecting corresponding points (*e. g.*, *B*, *C*, *D*), an area is encircled as in *III*, which represents the work-diagram. During every cardiac cycle this area is traced in counter-clockwise fashion. *A–B* represents the isometric contraction phase, during which the curve runs almost parallel to the axis, *P*. During the ejection phase (*B–D*), the curve becomes concave to the abscissæ. *D–F*, represents the isometric relaxation phase and *F–A*, the filling phase. From the fact that the curve is convex to the abscissæ, Straub concludes that a remnant of contraction process persists almost throughout diastole.

As in every machine, only a relatively small proportion of the total liberated energy is converted into mechanical work; the greater por-

[1] Wolfer (Arch. f. exp. Path. u. Pharm., 1922, **93**, 1) has recently attempted to record volume changes of the right and left ventricles separately. The results obtained indicate clearly that this is at most a very rough method and quite unsuitable for use in plotting cardiac work.

tion manifests itself as heat energy. The total energy of the heart beat may, therefore, be determined by adding to the mechanical energy, translated into calories, the heat liberated. The latter may be calculated from the oxygen consumption or liberation of CO_2. In

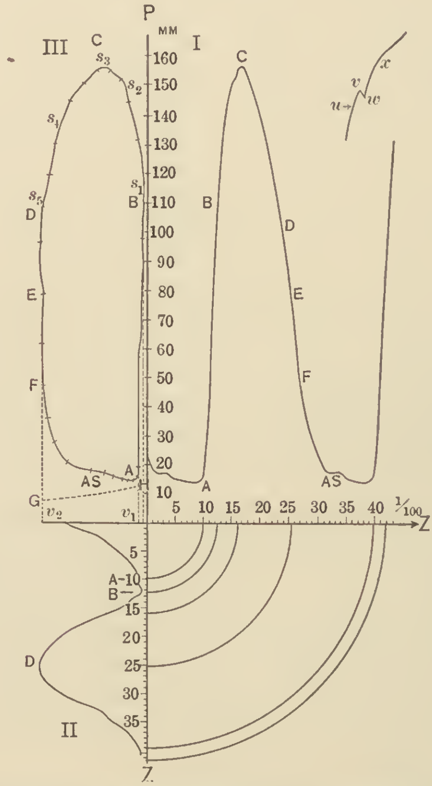

FIG. 47.—Method of constructing work diagram, *III*, from simultaneous intraventricular pressure curves, *I*, and ventricular volume curves, *II*. (After Straub.)

such ways the mechanical work was found to represent the following percentage of total energy exchange:

Evans (dog's heart)	1.3–20.0 per cent
Evans (dog's heart)	1.0–10.0 "
Evans and Ogawa (dog's heart)	3.0–11.0 "
Rohde (cats and rabbits)	2.9–25.8 "
Evans and Matsuoka (dogs)	5.1–19.7 "

It is obvious, therefore, that under optimal conditions the heart work corresponds fairly well with the mechanical efficiency of skeletal muscles, which are estimated at 20 to 25 per cent. These variations,

as the experiments of Evans and Rohde indicate, depend largely upon: (*a*) The venous return, (*b*) the arterial resistance and (*c*) on temperature.

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CHAPTER VI.

THE VASCULAR CONTROL OF THE CIRCULATION.

It is the function of the circulation not only to maintain an adequate and constant flow of blood through the capillaries, but to adapt the quantity to the physiological needs of the tissues. While the ventricular contraction supplies the primary motive power for accomplishing these needs, there are many conditions under which local variations of flow are necessary. This is accomplished by the peripheral vascular mechanisms. Not only are they necessary for this purpose, however, but it has been found that without their assistance the cardiac mechanism is quite incapable of maintaining an efficient circulation.

The Function of the Peripheral Arterioles.—Of greatest physiological importance are, perhaps, the smallest arteries and arterioles which immediately supply the delicate capillaries with blood. The smallest vessels opening directly into the capillaries are composed of endothelial cells and spindle-shaped muscle cells only, but more centrally they are divided into three layers—an inner endothelial, a middle muscular and an external elastic coat. The muscle cells, which are relatively numerous in these regions, are supplied by two types of motor nerve fibers—vasoconstrictors and vasodilators—capable of varying the caliber of these small vessels by increasing their contraction and relaxing their tonus. The peripheral arterioles may, therefore, be regarded as the stop-cock, controlling the flow of blood from the arteries to the capillaries, and are, furthermore, the chief physiological factors which determine the *peripheral resistance.*

We may first state, briefly, the generally accepted facts in regard to their innervation: The vasoconstrictor fibers are of the autonomic type. They arise from lateral horn cells situated chiefly in the thoracic region and emerge from the spinal cord from the second thoracic to the second lumbar region, reaching the sympathetic chain as preganglionic fibers. Here they terminate in some ganglion around ganglionic cells which send postganglionic fibers to the bloodvessels.

This vasoconstrictor mechanism is always tonically active, that is, the vessels are always partially contracted, as may be demonstrated by the fact that when any large nerve, such as the splanchnic, is cut a dilatation of the arterioles and a consequent decrease in blood-pressure results. This tonic activity does not, however, induce a maximal degree of contraction in the muscle fibers of the arterioles, for when such a nerve is stimulated a pronounced additional constric-

tion takes place with a consequent increase of arterial pressures, due to increased peripheral resistance (*cf.* page 123). It is still extremely doubtful whether the groups of cell bodies from which these fibers arise in the spinal cord may be regarded as a spinal center in the physiological sense. While it is true that section of the cervical cord is followed by a primary fall in blood-pressure and a subsequent recovery almost back to normal, critical experiments indicate that this recovery is due to other causes and that the spinal cells are relatively little, if at all, concerned (Yates). Nor is there any unqualified evidence that these cells can be reflexly modified under normal conditions; on the other hand, they are apparently capable of responding to changes in the gaseous content of the blood (Cathcart and Clark, Seppä).

The spinal cell bodies from which the vasomotor fibers arise are, however, influenced by fibers descending in the ventral and lateral funiculi (Ranson and Billingsby) which arise from cells located near the fovea inferior of the fourth ventricle. As stimulation of this spot produces an increased vasoconstriction and a rise of blood-pressure, this is designated as the *vasomotor center*.

The vasodilator fibers arise from cell bodies which are much more diffusely distributed throughout the central nervous system. Three groups of these fibers have been recognized: (*a*) Those which run in the parasympathetic system (*e. g.*, chorda tympani); (*b*) posterior-root dilators[1] (Bayliss) (*e. g.*, those supplying the limbs, skin, trunk, etc.), and (*c*) those of the sympathetic system. Considerable discussion has arisen as to whether these cells also are under the control of a chief vasodilator center in the medulla. Recent work to be presently analyzed indicates that this is the case.

The vasomotor center in the medulla has received considerable investigation; indeed, it may be considered a distinct chapter in the physiology of the circulation. It has been well established that, by virtue of its tonic activity, the peripheral arterioles throughout the body are kept partially contracted. This state of tone of the vasomotor center is partly due to chemical influences of the blood gases, but partly also to the continuous bombardment of afferent impulses (Stewart and Pike). Porter, on what appears to be quite inconclusive evidence, believes that the vasoconstrictor center, functionally at least, consists of two parts—a *vasotonic* and a *vasoreflex* center. Recent experimental evidence definitely inclines to the view that there is, in addition, a definite vasodilator center which does not, however, exert any tonic influence on bloodvessels, but is called into action on special occasions. The evidence in favor of this view is as follows:

1. Stimulation of the depressor nerve causes a vasodilatation not merely by reducing the tone of the constrictor center, but by in-

[1] For literature and recent experimental work relating to posterior root dilators, consult Ranson and Wightman, Am. Jour. Physiol., 1922, **62**, 392.

ducing an active dilatation in widely separated parts of the body. In view of the wide separation of the spinal cells, the control through a definite center seems probable (Bayliss, Fofanow and Tschalussov).

2. In the cat, at least, a point is found in the area postrema, about 3 mm. behind the vasoconstrictor center, where stimulation causes a vasodilatation and fall of blood-pressure (Ranson and others).

While these divisions of the vasomotor center are capable of being excited or depressed by changes in the vascular supply, changes in the composition of the blood, and possibly also by psychical impulses, it is chiefly a reflex center through which the blood supply of the tissues is controlled. It has long been known that either a general vaso-constriction or a vasodilatation may be reflexly induced (with a resultant rise or fall of blood-pressure) when afferent nerves are stimulated. This has quite generally been interpreted (Latschenberger and Deahna, Hunt) as due to the fact that afferent nerves are of two types, viz., those which excite a constrictor center (*pressor fibers*) and those which affect a central dilator center (*depressor fibers*). The evidence in favor of this view is briefly as follows:

1. Weak stimulation of most afferent nerves causes (quite independent of accessory influences, such as respiration, etc.) a reflex vasodilatation; strong stimulation, on the other hand, causes vasoconstriction.

2. Strong stimulation also causes reflex dilatation if nerves are cooled to 5° C. or during the process of regeneration.

Assuming that the pressor fibers do not react to weak stimuli, that their function is more affected by cold than is that of the reflex dilators or the depressor fibers, and that they regenerate less rapidly, all of the observed facts are readily and logically explained.

Considerable evidence has accumulated, however, which casts doubt on the existence of two specific types of fibers in afferent nerves (Ranson and associates, Martin and associates, Gruber). In the first place, the idea that different fibers are differently affected by cold or that they regenerate more rapidly is merely an assumption and not supported by the general known facts of nerve conduction. Furthermore, it is difficult to picture two afferent fibers so differently constituted that the stimulation threshold of one should be thirty times greater than that of the other (Martin and Lacey). In the second place, the results of quantitative stimulation indicate that the incidence of pressor or depressor effects (*i. e.*, reflex vasoconstriction or vasodilatation) is dependent on the number of fibers stimulated and the rate of stimulation. Thus, strong stimulation, inducing maximal impulses in all nerve fibers, causes a pressor reaction, while weak stimulation, affecting relatively small numbers of fibers (in accord with the "all or nothing" principle), induces only depressor effects (Martin and Lacey). Further, rapid stimulation rates (20 per second) tend to cause pressor responses whether the individual stimuli are weak or strong,

whereas slow rates (1 in two seconds) cause a lowering of blood-pressure even when the individual shocks are strong. According to these results, it appears that *the number of impulses arriving at the central nervous system in a given time determines the nature of the vasomotor response.* The effects obtained during nerve cooling and regeneration may be explained by the relatively small number of fibers transmitting impulses.

The studies of Ranson and Billingsby have shown that pressor and depressor impulses travel over separate intraspinal routes—the pressor fibers in tracts at the apex of the posterior horn (preferably homolaterally), the depressor fibers in the ventral part of the lateral funiculi (preferably contralaterally). On the hypothesis that the volume of impulses reaching the central nervous system determines the nature of the response, it is necessary to suppose that the depressor path is freely open to all impulse streams, but, owing to more complicated synapes, the pressor pathway is pervious only when large volumes of impulses are showered upon them.

Such an interpretation naturally carries with it the probability that when vasodilatation is replaced by vasoconstriction, this merely means that the greater activity of the vasoconstrictor center overwhelms that of the vasodilator (Martin). This is contrary, of course, to the conception generally held and supported by the work of Bayliss, Asher, Brücke and Hunt, viz., that a reciprocal action of the two centers exists, activity of the one being associated with inhibition of the other.

Reflex vasomotor effects are not only obtained by the stimulation of afferent somatic nerves, but from stimulation of afferent visceral nerves as well (Auer and Meltzer, Burton-Opitz, Davis). Apparently, both pressor and depressor reactions may be thus induced in different animals.

Reciprocal Cardiovascular Reflexes.—It has long been recognized (Marcy, 1860) that there is some sort of reciprocal relation between heart rate and vascular contraction: when the vessels relax, the heart accelerates; when the heart slows, the peripheral vessels constrict. The mechanism involved has gradually become clear. Increasing the pressure in the aorta causes a slowing of the heart, which is partly due to the increased blood-pressure on the cardio-inhibitory center, partly, however, to reflex stimulation of afferent fibers arising in the aorta (Eyster and Hooker; Brücke; Wickwire; Tournade, Chafrol and Marchand; Osborne). The active stimulus for such a reflex is apparently mechanical, *i. e.*, exerted by stretching of the aorta.

Conversely, when aortic pressure is reduced and the distention of the aorta is released—as happens when either the blood volume decreases or a peripheral dilatation occurs—a cardiac acceleration follows. This is only partly due to depression of the vagus center, partly to an active stimulation of the accelerator mechanism (Tournade, Chafrol and Marchand; Osborne; Wickwire).

A similar reciprocal response of the peripheral arterioles is generally supposed to operate when blood-pressures are altered by virtue of changes in cardiac rate or systolic discharge. When the arterial pressure falls either as a result of a decreased heart rate (peripheral vagus stimulation) or a reduced discharge (*e. g.*, changes in body position), compensatory peripheral constriction is interpreted as taking place, for upon return to normal conditions the actual pressures usually exceed normal. While this undoubtedly explains these changes in part, they may not be unqualifiedly explained in this way, for changes in systolic discharge undoubtedly occur under these conditions. Compensatory vasomotor activity thus resulting is partly referable to absolute or relative cerebral anemia, which increases the activity of the vasomotor center (Stewart and Pike, Sollmann and Pilcher, Tournade and others). That a reflex mechanism is also involved in this reciprocal adaptation of peripheral resistance to cardiac discharge is shown by the cross-circulation experiments of Tournade, Chafrol and Marchand, where the cerebral blood supply of the animal affected was kept constant and a reflex vasodilatation promptly followed an increased systolic discharge produced by the injection of serum. (For further examples *cf.* the reciprocal reaction during decreased circulatory volume in hemorrhage and shock, Chapter XXVI, page 583.)

Finally, mention must be made of a reflex mechanism by means of which increased volumes of venous return are pumped out by the heart to the arterial side. In addition to the direct mechanisms for accomplishing this (discussed in Chapter IV), it has been shown that a reflex cardiac acceleration also takes place (Bainbridge, Sassa and Miyazaki).

The Contractile Function of the Larger Arteries.—Since comparatively large arteries, such as the radial, brachial, femoral, etc., also contain muscle fibers, supplied by vasomotor nerves, the role that they play in the circulation must be considered. That their function must be essentially different from the "stop-cock action" of the arterioles is evident. Physiologists have generally considered these muscle elements either as functionless remnants or have regarded them as of service in adapting the caliber of the arterial system to the volume of the blood stream. Within recent years the possibility that they may take an active part in the propagation of the blood has again been actively supported (Hasebroek and Marês). The manner in which such an active factor in the propulsion of blood is supplied is conceived of as follows: During each systolic distention of the aorta by the ejected blood a local contraction of the central wall begins and spreads as a peristaltic wave, accompanying the pulse to the periphery. In other words, changes in diameter during each pulse beat are not entirely due to passive expansion in systole, but partly due to opposing muscular contractions. Some investigators

believe that this mechanism may not always be active, but held in reserve for special conditions, *e. g.*, when a large pulse volume is discharged (Marês).

Various arguments and experimental data have been presented, both in favor and in opposition to such an "active systole" of the arteries, as it has sometimes been designated by clinicians. The question is naturally asked, What may the function of these muscle fibers be if not to so assist the movement of blood? As already indicated, this has generally been answered by the statement that they may indeed cause gradual changes in volume which are of service in adapting the capacity of the vascular system to the blood volume. That a peristaltic contraction would in fact be capable, however, of aiding the onflow of blood, even if its occurrence be admitted, is very doubtful on a physical basis (Hess). While abundant evidence has been presented that excised rings of large arteries are capable, under certain conditions, of undergoing rhythmic contractions (Meyer, Günther, etc.), such contractions are those of slowly contracting smooth muscle and never occur as frequently as would be required to accompany the systolic pressure variation along the artery. Moreover, the velocity of the pressure transmission varies greatly under different conditions and would require the assumption of such changes in rate of conduction as are absolutely unknown in physiology. While rhythmic contractions have indeed been observed in smaller vessels and veins, neither observation nor cinematographic registration has given any evidence of their existence in the larger arteries of vertebrates (Hess). An observation of Hürthle, viz., that the established volume flow during systole and diastole is not proportional to pressure variations as calculations require, that the discrepancy is accentuated by vascular drugs known to cause muscular contraction (*e. g.*, epinephrin, pituitary extract) led him to ponder the question as to whether the unknown factor might not be such an active muscular contraction. These facts, however, have been much less critically interpreted by other writers (Marês) than by Hürthle himself, who finally reached the conclusion supported by others that definite evidence is not adduced by it in favor of an active propulsion of blood through arterial contraction (*cf.* also Hess, Fleisch). When it was shown (Blumfeld) that electrical variations accompany each arterial expansion, it was supposed to furnish definite evidence of active motor participation. Here, again, the failure to follow observations to their conclusion led to misinterpretation, for it now seems adequately established that such currents are of accidental physical origin and may be obtained quite as well in expanding lifeless tubes (*e. g.*, dead arteries, gelatin tubes, etc.). (Hürthle, C. Tigerstedt.) Finally, synchronous volume and pressure curves of arteries show that volume variations occur synchronously with and are equivalent to the pressure variations during every phase of systole and diastole (Fleisch). In view of these results, it may

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now be stated that not only is all evidence in favor of such an active systole lacking, but its existence is quite incomprehensible when the nature of nonstriated muscular contraction is taken into account.

The Functional Activities of Capillaries and Venules.[1]—The capillaries are generally described as consisting of a layer of bare endothelial cells and as being without connective tissue or muscular elements. A number of investigators, among them Golubew, Rouget and Mayer, have, however, described spindle-shaped cells lying upon and encircling the capillary walls in lower animals and believed that they possess contractile power. These observations have apparently been confirmed recently in Krogh's laboratory[2] and extended to small mammals (mouse, cat). While there is, therefore, evidence that some capillaries possess scattered contractile cells it may by no means be considered histologically demonstrated that they are present and active in all fully formed capillaries of higher mammals. Some of the differences of opinion regarding the presence of muscle cells may conceivably be due to the difficulty of clearly differentiating the transitions from capillaries to the smallest arterioles and venules. It is generally stated by histologists that the chief point of difference between capillaries and venules consists in the addition of a connective-tissue layer. According to Hooker, there is a sharp structural contrast between arterioles and venules, the former having muscular elements first appearing adjacent to endothelial cells, the latter having at first no muscular fibers but connective tissue only. As more central venules are approached, however, muscle fibers are also present.

Both capillaries and venules are supplied with delicate nerve fibrils and evidence of their active contraction has frequently been reported since the early observations of Stricker. Nevertheless, the idea has quite generally prevailed that, as far as the circulation of blood is concerned, these smaller vessels are entirely passive structures. It was not until the more recent investigation initiated by Krogh, Dale and Richards, Hooker and others that the nature and functional value of such contractions has been clearly indicated. It may now be regarded as fairly definitely established that these minute vessels are able to contract actively as a result of direct mechanical, thermal or electrical stimulation (Steinach and Kahn, Bruns and König, Ni, Carrier) and that a variety of chemical agents, among them CO_2, epinephrin, pituitrin, histamine, urethane and weak acids, are capable of causing an alteration in their caliber (Krogh and Rehberg, Carrier). Finally, experimental evidence has been presented to show that they are under nervous control as well (Hooker, Krogh). The importance of such independent contractile properties is of importance

[1] For literature previous to 1921, *cf.* R. Tigerstedt and Hooker. More recent articles dealing with structure, arrangement and function of capillaries and venules are listed in bibliography at end of chapter. *Cf.* also Chapter XVIII, page 393.

[2] *Cf.* Vimtrup, Ztsch. f. Anat. u. entwicklungsgesch., 1922, **65**, 150.

from several angles: (1) By virtue of their contractile and relaxing ability the number of functioning capillaries in any tissue may vary. This has been observed in muscle tissue (Krogh) and in the skin (Danzer and Hooker) as well as in the kidney glomerulus (Richards and associates). We may look upon this as a control of the blood stream in the vessels most intimately concerned with the nutritive and gaseous interchange of the tissues. In the active metabolic tissues the capillary channels, apparently close or open up in accord with the metabolic needs of the cells around them, furnish oxygen when asphyxia is imminent or divert supplies of blood to the places where it is most required. This is apparently accomplished largely by chemical stimuli locally formed as a result of metabolism. In peripheral tissues, such as the skin, however, which are exposed to continual harmful stimuli, the nervous mechanism probably controls their caliber. (2) By virtue of their tonic state of contraction and the complete obliteration of useless circuits, they prevent excessive quantities of blood from accumulating in the capillary areas and thus being withdrawn, in effect, from current circulation. The total capacity of the capillary bed when all are dilated is tremendous. While accurate determinations are, of course, difficult to make, the experiments of Dale and Richards indicate that when all are dilated to their maximum capacity (by histamine, for example) they are capable of accumulating so great a proportion of the circulating blood volume that the venous return of the heart is seriously interfered with, and the systolic discharge greatly impaired and the arterial pressure consequently falls to "shock levels." (3) Variations in capillary size share with that of the arterioles the importance of determining peripheral resistance. Nor do these mechanisms by any means operate in the same direction at all times; constriction of arterioles in association with relaxation of capillaries and venules is quite possible, at least under pathological and pharmacological conditions (Richards and Dale). In such cases the total peripheral resistance becomes the resultant of two opposing forces, and when this occurs we have evidence that the changed resistance in the capillaries may become the predominant factor. In this way, for example, Forward and Perme have explained how decreased arterial resistance in shock may occur coincident with increased vasoconstriction in the arterioles.

The total arterial resistance to the arterial outflow is, however, determined by still other factors, chief among which may be mentioned: (*a*) Variations in the viscosity of blood; (*b*) the variable extracardial support of capillaries and arterioles, and (*c*) the varying resistance offered by venous changes in venous pressure in advance of the venules. These factors will, however, be considered later (*cf.* page 151.)

The Venous Return of Blood to the Heart.—The Veno-pressor Mechanisms.—In order to eject sufficient volumes of blood, it is important that adequate volumes be returned to the right heart at all times.

As the minute volume of the heart varies greatly under different conditions, it is important that a mechanism should also exist whereby the volume of venous return is somewhat adapted to the volume discharged. Were this not so, the venous system would sometimes excessively overfill and at other times become excessively depleted.

The fundamental force responsible for the return of venous blood to the heart is, of course, the energy of systolic discharge. The volume of blood allowed to pass from the arterial to the venous side as well as the pressure under which it arrives in the smallest veins is, furthermore, determined by the peripheral resistance, a reduced resistance in the arterioles favoring a transfer of blood to the veins and a higher pressure; an increased resistance, on the other hand, diminishing both the venous pressure and the venous flow, owing to their increased capacity. In addition to these, other assisting mechanisms aid the return of flow. Among them may be mentioned the massaging action of muscular contractions which causes a centralward movement of the blood. Owing to the existence of venous valves, the synchronous abdominal compressions and thoracic suction during each inspiration act at once as a force and suction pump. In addition to these, Krogh has pointed out that the portal system, consisting of a double set of resistances and an intercalated reservoir with large capacity, acts as a general regulator of venous return. This is brought about by suitable adjustment of the splanchnic and intrahepatic systems analyzed in detail on page 157.

Of greatest importance in the return of venous flow is, however, the capacity of the smaller venules which is intimately linked with that of the capacity of the capillaries already discussed. The caliber of these vessels may be varied not only by changes in the contraction of their inherent muscle fibers, but also, to a considerable degree, by variations in the extravascular support they receive in muscular organs (*cf.* page 151). Henderson has referred to this as the *venopressor mechanism,* and is inclined to believe that it is controlled largely through chemical means, CO_2 being a normal hormone for the contractions of these vessels. Hooker, however, has presented evidence which indicates that they may also be under the control of nervous mechanisms,[1] which, in turn, may be set in operation by reflexes, as well as by chemical stimulation (*e. g.*, asphyxia). Henderson and Harvey have, moreover, shown that such reaction may occur quite independent of vasomotor arteriole changes. Thus, chemical changes which exert no effect on arterial pressure may cause great disturbance of venous pressure. Similarly, the great increase in venous return after epinephrin, when all arterioles are firmly contracted, is best explained by assuming that actions on the caliber of the venous systems is called into play (Connet) and may not be attributed, as Burton-Opitz believes, to a diminished systolic discharge.

[1] *Cf.* also Donegan: Jour. Physiol., 1921, **55**, 226. (Innervation of Superficial, Muscular and Mesenteric Veins.)

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CHAPTER VII.

THE CONTROL OF BLOOD FLOW THROUGH ORGANS.

THE quantity of blood passing through different organs is not constant from time to time, but alters, as a rule, with the conditions of activity. Thus, when the salivary or other glands secrete, when muscles contract and perhaps when increased nervous activity takes place, the blood flow augments. This may be brought about either by an alteration in the general pressure or by a change in the total peripheral resistance of the organ in question.

The Supplying Pressure.—When the total resistance in an organ remains constant and the pressure supplying that organ is intermittent, the mean pressure does not entirely determine the flow; but, on the contrary, the flow is proportional to the amplitude of the pressure variation (Hooker, Hamel, Gesell, etc.). The work of Gesell raises the question whether organs left intact within the body follow such simple dynamic rules, for he found that the flow through the kidney did not alter when the pulse pressure was reduced and the mean pressure remained the same. On the contrary, it sometimes slightly increased when the pulse pressure was reduced and the mean pressure fell. It is concluded from these results that the vascular resistance of intact organs alters to compensate for the change in pulse pressure.

The Total Resistance.—The total resistance in an organ is determined by the resistance offered to the flow by the venous pressure and by the friction between the blood and the vessel walls. This friction depends on the viscosity of the blood and the size of the vessels, as controlled, actively by nervous and chemical influences, and passively by extravascular support or pressure.

Thus, a high intraventricular or intracranial pressure may interfere with the flow through the heart or brain, respectively, and a great tonic contraction in muscular organs (for example, intestines and uterus) may entirely obliterate the vascular channels by compression. This is often the determining method of modifying peripheral resistance in muscular organs. In many organs devoid of such a mechanism (*e. g.*, glands) the active vasomotor constriction and relaxation of vessels determines the peripheral resistance. The presence of vasomotor fibers has been demonstrated for all organs, but their efficiency in controlling the blood flow is not equally developed in all regions. In fact, their activity has been so overshadowed by other factors that their presence in some organs has until recently

been questioned. This has been particularly so in the case of the cerebral and coronary vessels.

The evidence that the cerebral vessels are supplied with vasomotor fibers is partly histological and partly physiological. The vessels contain muscular elements. Nerve fibrils have been traced as far as their terminations in the cerebral vessels (Obersteiner, Huber, Gulland). That they are probably vasomotor rather than sensory fibers is evidenced by the following investigations of the writer:

1. When the isolated brain is perfused with a pulsating stream, the addition of adrenalin, which presumably acts on the sympathetic nerve terminals (Brodie and Dixon, Elliott, Dale) causes a diminution of flow through the organ (Wiggers). The criticism of the method made by Dixon and Halliburton has been answered by the writer, and, moreover, it has been possible to show that when the identical method of these investigators is used adrenalin still causes its typical constriction.

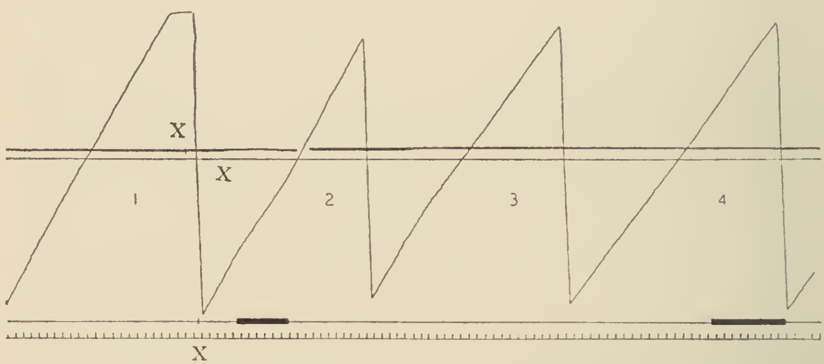

FIG. 48.—Curve showing by its change in slope the effect of stimulating the carotid sheath on the flow through the isolated brain.

2. If the nerve plexuses surrounding the carotid sheaths are stimulated at a time when the physiological condition of nerves and technic are favorable a decrease in flow through the brain vessels follows, as shown in Fig. 48. These results give *direct evidence of a nerve control over the cerebral vessels,* a conclusion foreshadowed by histological studies and the reaction to adrenalin. It may be pointed out that, owing to technical difficulties, negative evidence cannot counterbalance evidence of a positive character unless it can be shown that the procedures by which the latter was obtained were faulty. So far this has not been done.

Evidence of a similar kind favors the existence of a vasomotor supply to the coronary vessels. In the first place, fibers have been traced to the bloodvessels of the Purkinje system (Dogiel and others). In the second place a diminution of outflow from the right ventricle

of a perfused heart has been observed on vagus stimulation (Porter, Maas). These experiments, however, furnish "probable rather than quite conclusive proof" of a vasomotor influence. The factors affecting coronary vessels are so many and the communications of the vessels with the ventricle so numerous that any decrease or increase in outflow can be accepted as demonstrating vasomotor change only when it can be shown that: (1) The pressure supplying the coronaries remains the same; (2) the size of the right chambers existing as intermediary reservoirs is constant, and (3) the massaging effect of cardiac contractions on the intramural vessels has not altered. Recently, Porter has suggested another method of more accurately gauging the flow through the coronaries which is entirely free from these objections and should yield trustworthy results on stimulation. In the third place, adrenalin when perfused through a quiescent heart preparation invariably diminishes the coronary flow (Wiggers, Rabe). In the case of the beating heart, most investigators find that the flow is augmented (Schäfer, Wiggers, Morawitz and Zahn and F. Meyer, Markwalder and Starling). This the writer has attributed to the fact that the amplitude and rate (Markwalder and Starling) of beat increase, a factor that Porter has shown to augment the flow.[1] Brodie and Cullis found a similar reaction with large doses of adrenalin, but in the case of the smaller doses a decreased flow preceded this increase; and this they attributed to the constriction brought about by adrenalin.

It remains to consider the contradictory evidence offered by the fact that adrenalin usually dilates strips of coronaries immersed in Ringer's solution. This reaction has been repeatedly obtained in strips of the larger coronaries from the sheep, ox, goat, calf, etc. (Langendorff, Pal, Cow, Eppinger and Hess, Barbour, etc.). Barbour, however, found that the coronaries of man obtained at autopsy contracted. In harmonizing the constrictor action *exclusively obtained* in perfusing the resting heart with the dilator action found by the ring contraction method, it may be pointed out that the two methods test the reaction of different parts of the coronary system to adrenalin. The perfusion method tests essentially the reaction of the arterioles and capillaries and the ring method that of the larger arteries. The results are not necessarily antagonistic, but offer presumptive evidence that the larger vessels are supplied only with dilator fibers, while the smaller ones—and these are principally concerned with determining the blood flow through the organs—are supplied with both constrictor and dilator fibers. More direct evidence that the coronaries are influenced by vasomotors exists. Stimulation of the vagus nerve causes in the atropinized dog a decreased outflow from a wounded heart vein. This persists in spite of the fact that changes in the blood-pressure, the contraction of auricles and ventricles and backflow do not occur (Fig. 49).

[1] *Cf.* also page 156.

More recently, Morawitz and Zahn have interpreted the increased flow from the catheterized coronary sinus during stimulation of the stellate ganglion and its branches as indicating the existence of dilator fibers in the sympathetics. As they failed to control altogether changes in heart rate and arterial processes no significance can be attached to these experiments.

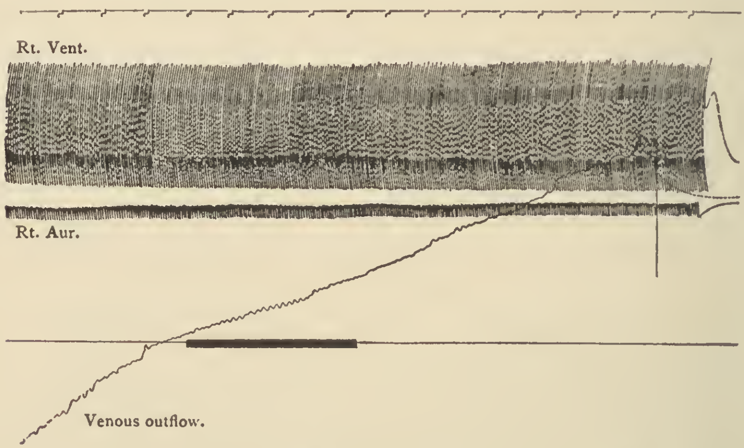

Fig. 49.—Effect of stimulating vagus (weak current) on the venous outflow from the coronaries when no change in the contraction of the auricle and ventricle was present (after atropine).

The Cerebral Circulation and its Control.—The brain is enclosed within the bony cranial cavity through certain openings of which arterial blood is admitted and venous blood passes away. Except for a few cubic centimeters of cerebrospinal fluid that may be displaced from the subarachnoid space into the spinal cavities, the brain is limited in its expansion. Hence the quantity of blood entering at any time cannot greatly exceed the outflow from the veins. This principle, first stated by Monro in 1783, has generally been designated as the Monro-Kellie doctrine.

The brain is supplied by the two vertebrals and the two internal carotid arteries, which form the basal anastomosing complex known as the circle of Willis. Recent evidence indicates that the functional anastomosis is less complete than the anatomical studies of Willis would indicate. Colored solutions injected into one vessel are distributed only to that section of the brain directly tributary to this artery, while drugs such as chloroform, which are harmless when injected into the carotid, act very powerfully on the respiratory and vasomotor centers when injected through a vertebral artery (Kramer). This is evidently due to the fact that the pressures are so evenly balanced that little or no intermingling occurs.

The blood returning from the brain substance is collected into the venous sinuses which are contained between folds of the dura and rest in grooves on the inner surface of the cranial bones. These sinuses drain largely through the lateral sinuses into the internal jugular vein, although numerous other collateral routes exist.

The cerebrospinal fluid surrounding the brain and large vessels is normally under a pressure equal to that of the veins (Bayliss and Hill). Under abnormal conditions it may rise considerably. When this occurs the veins are not obliterated, as might be expected, and a self-strangulation does not occur. The flow is not reduced until a pressure nearly equal to intra-arterial is attained. This is probably due to the protection which is afforded to the veins by the inelastic dura. It is only when the pressure becomes high enough to compress the unprotected arteries that the flow is reduced. Were it not for this protection an increase in general blood-pressure, by expanding the cerebral arteries and raising intracranial pressure, might compress the veins and reduce the outflow, as was at one time claimed by Geigel and Grashney.

It has been conclusively demonstrated that the cerebral circulation in experimental animals follows in every essential phase the variations of the general arterial pressure. When the arterial pressure rises the volume tends to increase if a trephine opening is made, the intracranial, intra-arterial and intravenous pressures increase and a larger flow of blood through the brain occurs (Roy and Sherrington, Bayliss and Hill, Gaertner and Wagner, etc.). There is no reliable evidence that the vasomotor fibers demonstrated to be present are powerful enough to overcome any considerable variation of general arterial pressure. Of this one can convince oneself directly by perfusion experiments. If a constriction is induced by adrenalin it requires only a very slight elevation of the perfusion pressure (5 mm. often suffices) to annul it, whereas in other organs, as the kidney, a pressure rise of 40 to 50 mm. will not overcome the constriction. These nerves clearly play very little part in modifying the bloodflow through the brain. Their function is as yet unknown. The possibility exists, as Howell suggests, that they may serve to adjust the distribution of blood within the cerebral areas by directing blood in larger quantities to those regions undergoing special activity. It is not impossible that they are in some way associated with or perhaps responsible for sleep, for, according to Shepard, the volume of the brain increases during this act.

The Coronary Circulation and its Control.—The heart muscle receives its blood supply from the two coronary arteries which break up into intramuscular capillaries. From these regions blood is collected by venules and veins which finally empty into the coronary sinus of the right heart. There are, however, direct communications with the ventricles by means of the Thebesian vessels, which, as

Pratt has shown, are efficient vascular channels in the nutrition of the heart.

The flow through the coronary system is dependent to a marked extent on the arterial pressure. The height of blood-pressure, as a rule, overbalances any active vasomotor changes. Thus, if a general vasoconstriction, of which the coronary vessels partake (for example, after adrenalin), is induced and the blood-pressure is raised in this way the flow through the heart will increase. This has been shown in perfusion experiments as well as in hearts intact within the body (Markwalder and Starling, Morawitz and Zahn, Bard, personal observations).

The flow is modified also by the activity of the organ itself, that is, by its rate and amplitude of contraction, its tonus and the height of intraventricular pressure (Magrath and Kennedy, Hyde). With each beat blood can be seen to be forced from a cut vessel. This is due to the fact that during systole muscular contraction compresses the intramural vessels and forces blood onward in the direction of least resistance, and during diastole the emptied vessels are quickly refilled by the greater pressure in the central arteries.

Consequently, it may be inferred that an increased rate of beat tends to increase the rate of flow in a mechanical way. This was actually found true by Porter and substantiated by the author in the case of hearts which were perfused by constant pressures and from which the total coronary flow was collected. The recent experiments of Nakagawa, on the contrary, indicate that changes in heart rate are almost *without* effect on the flow from the coronary sinus alone, while Morawitz and Zahn report that tachycardia actually decreases the flow. It is not clear, however, that coincident changes in ventricular tonus or alteration in intraventricular pressures were taken into account.

This varied control of the coronary flow is well adapted to adjust automatically the volume of coronary blood flow to the needs. Thus, whenever the rate of the heart increases the blood supply is augmented, not only through the elevation of aortic pressure but by the more frequent recurrence of muscular compression of the vessels. When the systolic discharge increases the aortic pressures are similarly elevated and the more powerful contraction of the musculature alternately increases the blood flow during systole. Furthermore, it has shown (Markwalder and Starling, Morawitz and Zahn) that chemical substances such as epinephrin, CO_2 and other products of metabolism increase the coronary flow, results which have been boldly interpreted as indicating an active dilatation of the coronary vessels. A critical examination of such experiments does not permit one to say, however, that these effects were not induced by a direct mechanical effect of the increased cardiac activity resulting from these chemical substances, *e. g.*, by changes in rate, amplitude or tonus.

The Circulation through the Liver and its Control.—On account of its very important functions associated with digestion and nutrition, the liver is favored with an exceedingly great blood supply. With the exception of the lungs, the liver receives the largest total supply of any organ in the body. It has been estimated (Burton-Opitz) that a liver weighing 500 gm. in a dog weighing 15 kilos receives 420 cc of blood per minute; or, roughly stated, an amount of blood equal to the entire amount in the body traverses the liver every three minutes.

It receives this supply from two sources—the hepatic artery and the portal vein. The arteries not only supply the walls of the bile ducts and the portal vessels, the connective-tissue capsule and trabeculæ, but also communicate with the radicals of the portal system, so that a mixture of arterial and venous blood reaches the capillaries. The arterial and venous branches join at an acute angle (Gad), forming a sort of valve which may shift in accordance with the pressure on each side.

Stromuhr experiments (Burton-Opitz) indicate that more than two-thirds of the total liver flow comes from the portal side, which, in turn, derives its greatest supply in the order named from the intestines, stomach, spleen and other splanchnic organs. This relation exists in spite of the fact that the hepatic artery has a pressure not materially lower than that in the aorta, while the portal vein has a pressure equal to about 10 mm. of mercury.

It is evident that the flow through the liver may be passively modified, not only by variations of arterial pressure, but also by changes in the portal pressure, which is determined by the flow through the abdominal organs. Thus, a marked constriction of the vessels of the intestines, spleen, etc., causes an elevation of pressure in the aorta and hepatic artery, but a decrease in portal pressure. It is desirable to determine the result of such vasoconstriction on the arterial and venous flow through the liver. Inasmuch as the splanchnic nerves apparently are not connected with the postganglionic vasomotor fibers for the liver (Burton-Opitz), it is possible to do this by stimulation of the splanchnic nerves. When this is done the portal flow first increases and the pressure rises, due to the onward movement of blood into the central portal veins. This is soon followed by a reduced flow and a fall of portal pressure. This is compensated for, however, by an increased inflow passively brought about by the rise of pressure in the aorta. The hepatic artery serves as a compensatory mechanism in such cases, ensuring an adequate supply to the liver.

A different situation results, however, when the portal flow is mechanically shut off or reduced. The arterial flow then does not increase in a compensatory manner, as might be expected, but is likewise reduced. The reason for this is that when the portal supply is shut off less blood is returned to the heart, and in consequence the arterial pressure falls. The flow through the arterial channels

of the liver is then determined largely by the height of the arterial pressure.

The question remains whether the pressure within the portal vessels and the flow may also be modified by venomotor nerves. It is generally held, after the experiments of Mall, that the portal vein is supplied with such a special vasomotor control which may regulate the flow independent of other organs. While some experiments have not favored the idea that such a control exists (Velich, Marês), its existence and significance have been definitely established by the recent work of Burton-Opitz.

Having recognized the dependence of the liver volume on arterial and portal pressure, it is necessary to consider the arterial vasomotor regulation. It has been shown that stimulating the nerve strands, passing from the celiac ganglia with the hepatic trunks to the liver, causes a marked rise of arterial pressure and a reduction in arterial flow. In the case of some fibers this amounts to almost a complete cessation. While the arterial inflow is thus reduced, due to vasoconstriction, the portal flow suffers only a slight reduction, which indicates that the fibers distributed to the venous radicals act feebly as compared to those supplying the arterial branches.

Since nerve stimulation does not markedly modify the flow of portal blood, it seems that this flow is largely dependent on the vasomotor mechanism in the organs tributary to the portal vein. The fact, however, that the flow diminishes after the introduction of adrenalin indicates that a contraction of the intrahepatic radicals of the portal vein occurs. The exact location of this mechanism is, however, as yet undetermined (Burton-Opitz).

As the portal vein lies between two sets of capillaries, those of the mesenteric arteries, on the one hand, and those of the liver, on the other, the regulation of portal pressure is determined largely by the relative inflow and outflow per unit time. The inflow is controlled largely by the arterial pressures and the caliber change of the vessels innervated by the splanchnic nerves; the outflow is similarly regulated by the caval pressures and the caliber of the intrahepatic veins and capillaries. Until recently, however, pressure determinations have limited themselves to the establishment of mean pressure variations, and the impression has been that the pressure variations were fairly constant during systole and diastole. Recently, Feil and Forward have shown, however, by optical registration, that a definite portal pulse exists. Typical variations at rapid heart rates are shown in Fig. 50. In general, the pressure falls during systole and rises to a rounded summit during diastole. The systolic fall, however, is interrupted by a sharp peak which occurs almost simultaneously with the peak of the abdominal aortic pulsation, and this is followed by a sharp decline. With greater detail we may describe the curve as follows: At the exact instant that systole begins (as indicated by the

large vibration of the first heart sound) the curve has already begun to decline gradually. This gradual decline, however, is interrupted by a sharp peak, *b*, after which it falls abruptly to a trough, *c*.

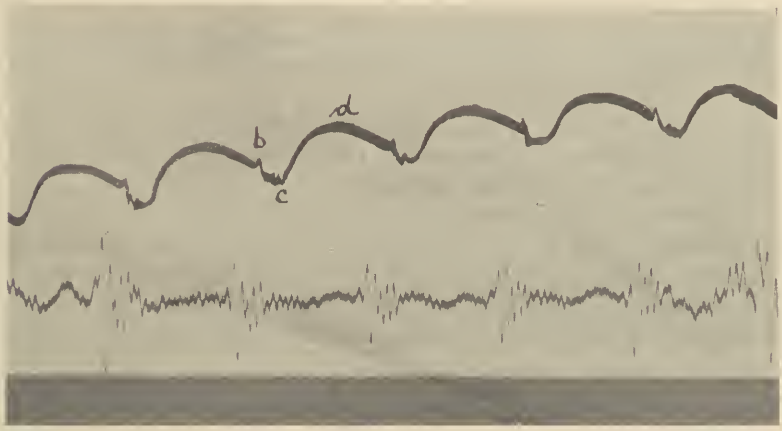

FIG. 50.—Portal-pressure curves (upper) and heart sounds (lower) during moderate saline infusion, showing augmentation of the main wave, *d*. (After Feil and Forward.)

Then the upstroke of the main wave, *d*, commences. The beginning of this rise precedes slightly in early vibrations of the second heart sound; in other words, it begins in late systole and is continued well into diastole, so that the crest of the wave is approximately mid-diastolic. From the crest the curve declines until the next systole

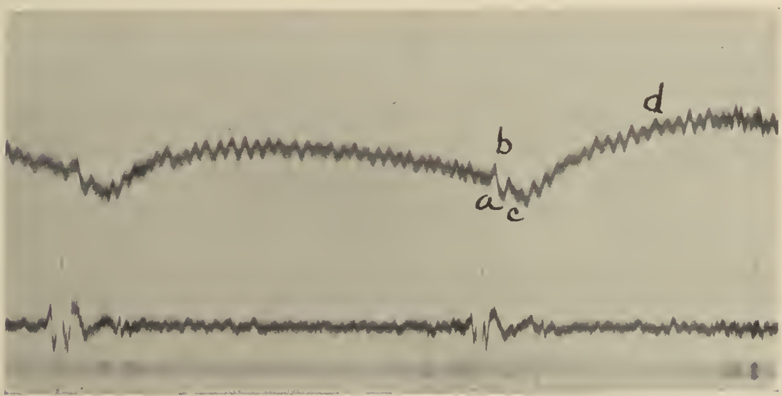

FIG. 51.—Portal-pressure waves during vagal slowing. (After Feil and Forward.)

occurs and the cycle is repeated. The prominence of the diastolic wave, *d*, is determined by the volume of the systolic discharge, being decidedly increased after a moderate infusion. When the heart slows

to rates comparable to those in man, the significance of these pressure variations become even clearer. This is shown by the curve of Fig. 51. The most obvious difference is that the summit of the *d* wave is followed by a more prolonged diastolic fall not present in rapid rates. The entire wave consequently appears of larger amplitude, its summit being either rounded or flat. Time relations show, however, that the summit, *d*, occurs approximately at the same time after the end of systole. The fact that it is no longer in mid-diastole is entirely due to the greater prolongation of diastole, which gives opportunity for a subsequent diastolic fall to express itself more clearly.

In endeavoring to interpret the cardiac variations in portal pressure, it is important to bear in mind that the portal pressure at any moment is determined by the balance between the inflow of blood through the splanchnic capillaries and the outflow through the liver capillaries. Whenever the portal pressure is on the increase inflow exceeds outflow, and, *vice versa*, whenever the portal pressure declines outflow exceeds inflow.

With every systolic increase of pressure in the tributaries of the mesenteric arteries a larger pulse volume is sent through their capillaries into the portal vein. Owing to the relatively great capillary resistance the entrance of this volume pulse into the portal system is somewhat delayed. This accounts for the elevation of pressure late in systole and its continued elevation in early diastole (*c–d*, Fig. 50). Occasionally, as in Fig. 51, a stable equalized condition obtains for a short while, accounting for the flattened summit of *d*. Then follows a state where outflow exceeds inflow, due, no doubt, to the fact that the portal vein receives a smaller quantity of blood as the arterial pressure falls during diastole. Consequently, the portal pressure then falls definitely during the remaining portion of diastole. If the heart is rapid, diastole is short and the next systole supervenes before this fall has had time to express itself. Consequently, as in Fig. 50, the pressure continues to rise almost throughout diastole and falls during systole. Were these the only factors determining portal pressure variations during systole and diastole, we should expect the curve to show an unbroken fall during early systole. Actually, we find a small peak, *a–b*, followed by a sharp drop, *b–c*, at the beginning of systole, occurring 0.04 to 0.06 of a second after the first sound, while the depression, *b–c*, begins slightly before or with the rise of pressure in the abdominal aorta at its bifurcation. In the interpretation of these sharp variations, *a*, *b* and *c*, it is difficult to conceive of any sudden change in outflow or inflow sufficiently rapid to cause this acute change in pressure. The rise and fall of this wave may, therefore, be most satisfactorily explained as due to an extraportal impact or traction effect.

Relative Vascular Supply of Different Organs.—As the volume of blood supply depends on the intensity of metabolic activity, it may

be supposed, on *a priori* consideration, that their blood supply during activity and rest varies. Furthermore, blood serves different purposes in different organs. In the nervous system and muscles, for instance, it essentially supplies the material for maintaining their activity and offers an avenue for the disposal of waste products. Other organs, however, modify or regulate the composition of the blood, either, as in the lungs or intestines or glands of internal secretion, by adding new substances to it or, as in the kidney, by removing waste products of metabolism. A knowledge of the relative and absolute blood supply of different organs is not only of interest from the viewpoint of the circulation, but also in understanding the metabolism of the body, since it may be assumed that the share taken by different organs in the total metabolism is proportional to their blood supply, per unit time, per 100 gm. of that organ. The following table, copied, with few exceptions, from Burton-Opitz, gives an idea of the relative vascularity of different organs of the body as determined by inserting a stromuhr into the arteries furnishing blood to the organs:

Minute Volume per 100 Grams Substance.

	cc.	
Posterior extremity	5	Tschuewsky.
Skeletal muscles	12	Tschuewsky.
Heart	16	Bohr and Henriques.
Head	20	Bohr and Henriques.
Stomach	21	Burton-Opitz.
Liver (arterial)	25	Burton-Opitz.
Portal organs (combined)	30	Burton-Opitz.
Intestine	31	Burton-Opitz.
Spleen	58	Burton-Opitz.
Liver (venous)	59	Burton-Opitz.
Pancreas	80	Burton-Opitz.
Liver (total)	84	Burton-Opitz.
Brain	136	Jensen.
Kidney	150	Burton-Opitz.
Suprarenal	490	Burton-Opitz.
Thyroid	560	Tschuewsky.
Thyroid	355	Knowlton, Dooley and Curtiss.

It is of interest to notice that the liver, with its large mass and varied functions, takes a place subordinate to such organs as the brain, kidney and thyroid when calculated on a basis of unit mass.

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CHAPTER VIII.

THE PHYSIOLOGY OF THE PULMONARY CIRCUIT.

THE pulmonary system differs from the systemic in several essentials: It is a relatively short circuit in which the vessels subdivide much more rapidly and in which the resistance to peripheral flow is very much less. The vascular walls are comparatively thin, and though supplied with muscle fibers and nerve fibrils (Larsell), their tonic activity is apparently not highly developed.

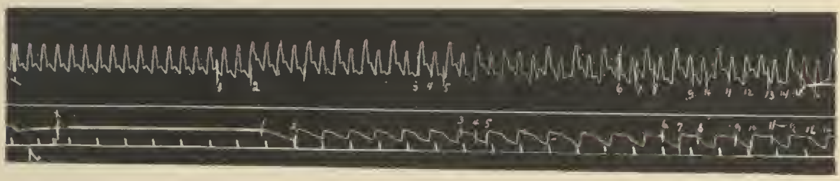


FIG. 52.—Pulmonary arterial pressures (upper) and respiration (lower) in naturally breathing animal—showing effect of apnea and inspiration.

Pulmonary Pressures.—This relatively low arterial resistance is largely responsible for the fact that the pressures in the pulmonary artery are relatively low and in the pulmonary veins and left auricle somewhat higher. Tabulations compiled by R. Tigerstedt show that when the chest is opened the mean pressures average 12 mm. Hg. in the rabbit, 18 mm. in the cat and 20 mm. in dogs, and similar values have been more recently added both in closed and open chest experiments. (For reference *cf.* Wiggers, *Physiological Reviews.*) When the chest is closed marked variations of pressure occur in the pulmonary arteries with each phase of respiration (Plumier, Schäfer), and more accurate measurements show that both systolic and diastolic pressures fall during inspiration and rise during expiration, the pulse pressures being greater during the latter phase. As in the systemic circuit, the pressor influence of respiration affects these pressures. Thus, during apnea the systolic pressure is reduced and the average diastolic pressure is elevated (Fig. 52). During natural respirations the author found that the maximum systolic pressures average 43.3, the minimal diastolic pressure 11.9 mm. During phases of respiration an average variation of 12 mm. in systolic pressure and of 8 mm. in diastolic pressure was found.

Comparing these results (Fig. 53) with the variations in the sys-

temic circuit, it is evident that while both systolic and diastolic pressures range much lower in the pulmonary vessels, the respiratory fluctuations are actually as great and in some instances larger. The mechanical action of respiratory movements contributes approximately 32 to 40 per cent to the height of the maximal pressure and depresses the minimal pressures 10 to 20 per cent. In other words, during apnea the maximal pressure falls and the minimal increases. Presumably, the mean pressure is little affected.[1]

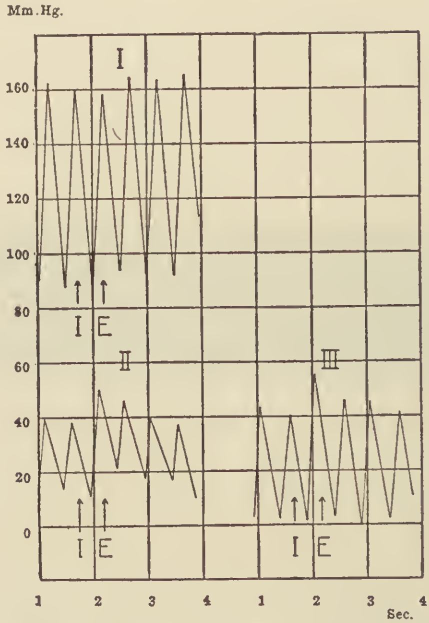


FIG. 53.—Diagram showing the respiratory variations of systolic and diastolic pressure in the right ventricle, *I*, pulmonary artery, *II*, and carotid artery, *III*.

The Nature of the Pressure Variations.—As in the systemic circuit, the variations in pressure may be described as cardiac and respiratory.

The contour of the cardiac variation resembles that obtained by Frank in the aorta, the chief difference being that the summit is reached relatively early in systole (Fig. 54). The wave, *A–B*, evidently corresponds to the auricular contraction. In many cases this is followed by an elevation, *B–C*, before the negative wave, *C–D*, supervenes. This, in turn, is followed by the short vibration, *D–E–F*, after which the main rise occurs. A study of curves enlarged and transcribed to millimeter paper after a method similar to that described by Brömser leads to the conclusion that the true isometric period

[1] For details *cf.* Wiggers: Am. Jour. Physiol., 1912, **30**, 248.

falls during the waves *C–D–E–F* and that the wave *B–C* when present is concerned with auricular pressure changes. The negative wave, *C–D*, present in the aortic curve only during low pressure is always clearly distinguished in the pulmonary arterial record. Although the diastolic pressure in the pulmonary artery is much lower than that in the aorta the isometric period is not materially different from that in the left ventricle.

Following the preliminary vibrations and the opening of the semilunar valves the pressure rises suddenly to *G* and rapidly falls to *H*. Since the vibration period of the primary pressure wave of *G* equals about 0.03 second and the inherent period of the instrument was 0.00636, it must evidently be attributed to a vibration of the blood column existing within the artery and not to an instrumental vibra-

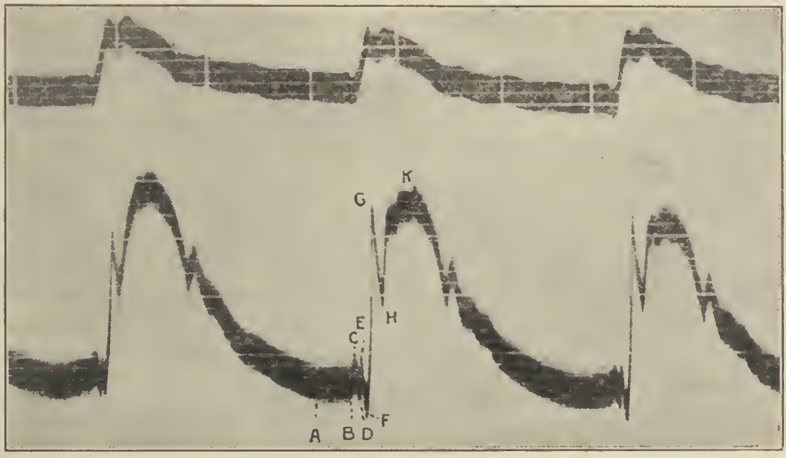


Fig. 54.—The details of the pressure changes in the pulmonary artery (lower curve) during inspiration and expiration.

tion. In all the records the amplitude of this vibration is much greater than in the systemic circuit. Following the primary wave, the record assumes a rounded top which may be regarded as the true systolic summit and then rapidly falls to the incisura. In the experiment from which the waves of Fig. 54 were taken the right auricular pressure was 14 mm. of water during expiration and —15 mm. during inspiration, pressures which may be regarded as normal, inasmuch as they agree favorably with pressures found in unanesthetized animals. In order to study the effect of increasing the venous pressure, saline was slowly infused by the jugular. When the pressures reached 68 to 80 mm. above intrathoracic a pronounced increase in amplitude occurred and the curve assumed the form shown in Fig. 22, *A*.

In naturally breathing animals important changes, not only in the

height, but also in the details of contour, occur during inspiration and expiration. Their essential character is shown in the consecutive waves of Fig. 54, the first of which occurs during expiration and the last two during inspiration. Inspiration at its beginning causes a descent of the diastolic portion of the second curve, which is followed by a proportionate fall of systolic pressure (measured at the height of the rounded curve), so that the pulse pressure is not greatly reduced. In the third wave, however, occurring at the height of inspiration, the systolic pressure is markedly lower and the pulse pressure is much reduced. Corresponding changes in the height of the carotid curve take place. The contour of the inspiratory pressure wave (second wave) differs from that of expiration (first wave). During inspiration the auricular wave is less prominent, but the amplitude of the preliminary vibration, *D–E–F*, becomes much greater. The time relations remain unchanged. The primary upstroke, *G–H*, also becomes larger and sharper in its rebound, and after its completion returns more rapidly to the top. The systolic summit which was smoothly rounded in expiration approximates a short ascending or horizontal plateau. These changes can be explained by a decreased resistance in the pulmonary vessels.

More extended observations show, however, that systolic and diastolic pressures fall in this manner in inspiration only when not more than two beats occur during that phase. Should a third beat occur, the systolic pressure increases again in spite of the fact that the diastolic pressure remains low (Fig. 55). A study of the intraventricular pressure curve indicates that this increase is accounted for by an increased systolic discharge. Furthermore, the ratio of the heart and respiration rates (*H:R* ratio) and the apportionment of the heart beats to the respiratory phases determine the pressure relations. When the phase of expiration is separated from succeeding inspiration by a period of respiratory rest and the acts of inspiration and expiration begin exactly at the systolic upstroke, then (*a*) inspiration reduces the systolic and diastolic pressures of the first and often the second wave, but *occasionally* the second and *generally* the third wave show an increase of systolic pressure; (*b*) the act of expiration always elevates both systolic and diastolic pressures above the last inspiratory pressures; and (*c*) during the phase of expiratory rest both pressures progressively fall until the apnea level is reached (see plots I, II, III and IV of Fig. 55). When inspiration begins during diastole, the diastolic pressure is immediately decreased and the systolic pressure of the next wave materially reduced, so that the pulse pressure is smaller. When expiration starts during diastole, the diastolic pressure is immediately augmented and apparently offers a support to the next wave, which reaches a high summit (plot V, VI of Fig. 55 and waves 6, 7, 8, 9, 10 and 11 of Fig. 52). When inspiration and expiration gradually merge into each other, both systolic and diastolic pressures

fall for two beats or so in inspiration, but if more beats occur the systolic pressure rises again. During expiration both pressures rise greatly during its early portion, but subsequently fall again toward the end of expiration (plots VII, VIII of Fig. 55, also Fig. 66).

During expiration both systolic and diastolic pressures are increased, the diastolic often elevating during the period when the semilunars are closed. This is apparently traceable to an increased pulmonary resistance in the deflating lungs and also to an augmented systolic discharge.

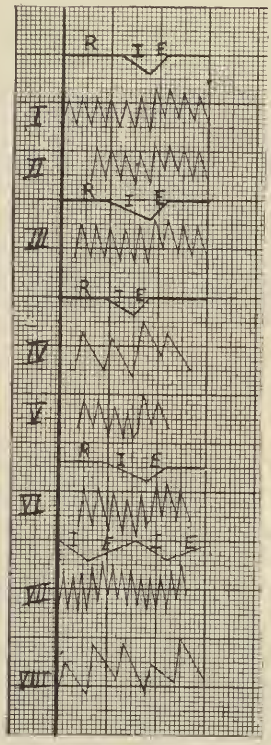


Fig. 55.—Plots from optical tracings, showing the effects of different heart-respiration ratios on systolic and diastolic pressures.

The variations of pressure in the pulmonary veins have not as yet been satisfactorily investigated in the closed chest. In the opened chest the mean pressure equals only a few millimeters of mercury. Probably the pressure in the closed chest differs only a trifle from that in the left auricle. Experiments have shown that the actual left auricular pressure is usually negative during inspiration (−2 to −50 mm. saline), but, as a rule, becomes positive during expiration (+6 to +38 mm. saline). The effective pressure, *i. e.*, the difference between

left auricular and intrathoracic is slightly greater in inspiration than in expiration, (51.1 mm. saline as compared with 46.4 mm.).

This great drop in pressure gradient between the pulmonary artery and left auricle is largely due to the fact that the left heart keeps the pulmonary veins well pumped out, and, in consequence, the left heart unlike the right does not enjoy a luxus supply, but is dependent at all times upon the right heart for an adequate supply.

The Mechanical Control of the Pulmonary Circulation.—Three mechanical factors, operating separately or together, may conceivably alter the pressures and volumes of blood contained in the pulmonary vessels. They are: (1) The minute output of the right ventricle; (2) the resistance and capacity changes in the pulmonary circuit; (3) "back-pressure resistance" produced in the left heart by changes in the systemic circuit.

1. *The Minute Output of the Right Heart.*—The minute volume discharge from the right ventricle into the pulmonary artery is determined by the heart rate and systolic discharge.

The systolic discharge, as determined by the volume of venous return, within wide limits determines pulmonary arterial pressures and the volume flow, provided, of course, that other factors remain equal and that dilatation and decompensation stages are not arrived at (Erikson, Cloetta and associates, Fühner and Starling, etc.). As regards heart rate changes, it has been pointed out that within normal ranges, surprisingly small variations in systolic and pressures occur. As the heart cycle increases in length up to 0.8 second (approximately), the systolic pressure either undergoes no change or displays a slight tendency to increase. When the cycles exceed one second in length the systolic pressure actually increases. *Pari passu* with these changes the diastolic pressure undergoes a reduction (Fig. 56). This does not signify, however, that the volume flow is unaltered, but, on the contrary, the flow from the pulmonary veins decreases, as shown in Fig. 57, when the heart is slowed by vagus stimulation or by drugs acting on the vagus center.

Interesting observations as to the pulse flow in the smaller vessels have recently been made by Hall[1] by direct inspection of the vessels of a transilluminated lung. When a marked cardiac slowing obtains, the flow in the smaller arteries is backward during diastole and becomes stationary during systole until a new pressure equilibrium is reached in the pulmonary aorta. As soon as this obtains, a slow onward movement is obtained. All of these facts indicate that while the pressure variations are not greatly affected by a cardiac slowing, this does seriously affect the volume of blood flowing through the lungs. Plethysmographic registrations, furthermore, indicate that the volume of blood contained in the lungs is increased as the heart slows (Weber,

[1] As yet unpublished experiments carried out in the Physiol. Lab. of West. Reserve Med. School.

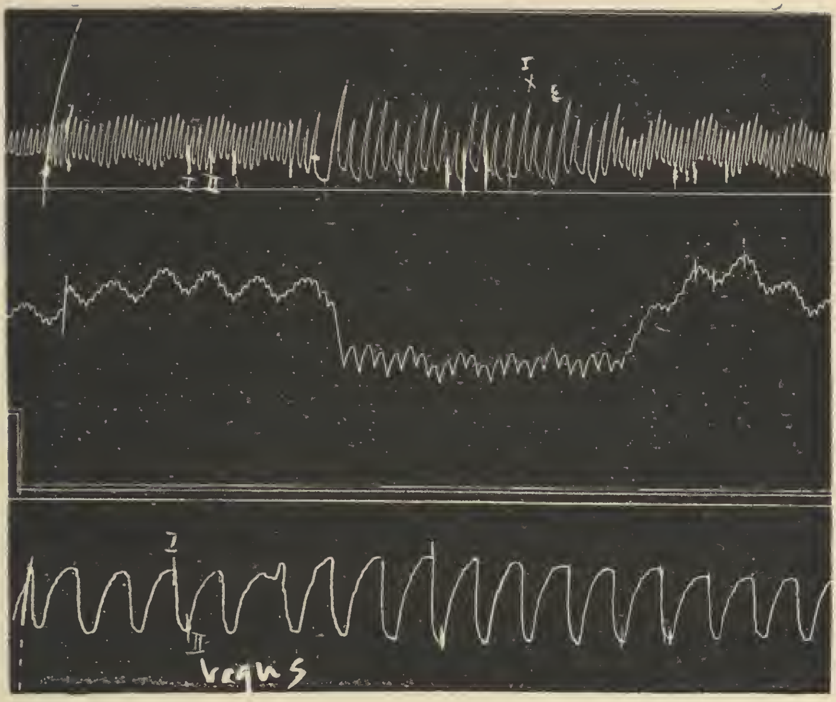


FIG. 56.—Pulmonary arterial pulse pressures (upper) mean carotid pressure (middle) and natural respirations (lower), showing the effect of breathing without expiratory pause when heart-respiration ratio is great and small (vagus stimulation).

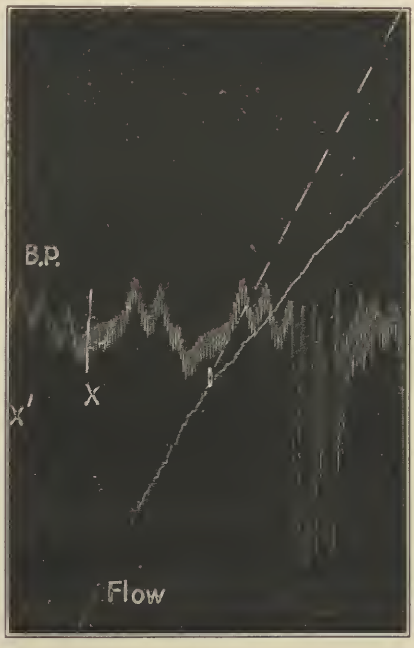
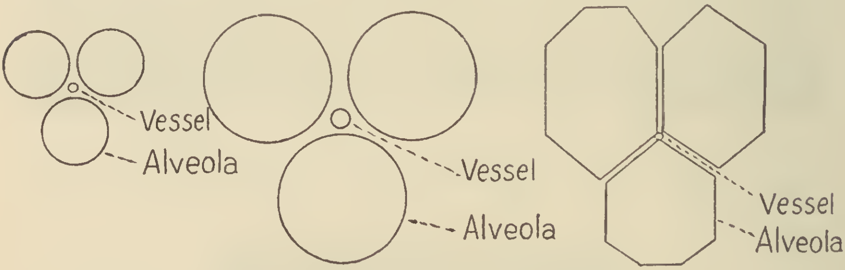


FIG. 57.—Effect of decrease in heart rate consequent to vagus stimulation on the blood flow through the pulmonary vein. x–x', relative positions of points.

Anderes and Cloetta). This might be interpreted to indicate that while the volume of pulmonary venous blood increases, the volume of arterial blood decreases.

2. *The Resistance in the Pulmonary Circuit.*—When rate and output are constant then the total peripheral resistance may modify the flow through the lungs; an increase in resistance, raising both systolic and diastolic arterial pressures and reducing the volume flow.

By the total pulmonary resistance we mean the sum of all the resistances that impede the flow through the lungs. It is governed: (*a*) By the degree of lung expansion, (*b*) by the effect of negative pressure on the extrapulmonary vessels, (*c*) by vasomotor variations, and (*d*) by an altered *vis a fronte* caused by impaired action of the left heart. We may take these factors up separately. It has recently been pointed out (Cloetta) that as the lung expands two opposing factors act upon the intrapulmonic vessels. When first the alveoli expand they tend to exert a radical traction upon the small vessels



A *B* *C*

FIG. 58.—Diagrams illustrating the effect of lung inflation on the alveoli and lumen of the intrapulmonary vessels. *A*, collapsed lung; *B*, moderately inflated lung causing larger lumen by radial traction; *C*, marked inflation causing compression by virtue of polygonal shape of alveoli. (After Cloetta.)

and capillaries and so enlarge them, but as the enlargement proceeds and the alveoli acquire a polygonal shape, they tend to compress the intrapulmonic vessels (Fig. 58). Furthermore, as the lungs enlarge they necessarily cause a linear extension of the bloodvessels and thereby further reduce their caliber. From this it appears that a moderate distention of the lungs causes a diminished resistance, but an extreme distention, an augmented resistance.

It can readily be shown that the capacity of the large extrapulmonary vessels may increase when the surrounding pressure becomes more negative. This influence is exerted more upon the large pulmonary veins than upon the arteries (de Jager). It is probable that the mechanical variations of resistance of the intrapulmonary as well as the extrapulmonary vessels play an important rôle in creating the respiratory variations in pressure in the pulmonary circuit.

Whenever the output of the right heart increases, whether due to a

different venous pressure or to an inherent influence modifying the contraction of the heart, the pressures increase in the pulmonary artery and the flow augments. This increase in pressure and flow also extends to the pulmonary veins, even when the heart rate is somewhat slowed and the lung vessels tend to actively constrict as they do after adrenalin. It appears that *a change in the total peripheral resistance is practically without influence on the pulmonary circuit when the change opposes the cardiac output in its effect.*

3. *Back-pressure Effects.*—If, even for a few beats, the minute discharge of the left heart is reduced while that of the right heart remains unaltered, a stasis of blood within the pulmonary veins must take place. By offering greater resistance to the normal flow of capillary blood, this increased *vis a fronte* tends to elevate the pulmonary arterial and right ventricular pressures also. This dynamic sequence is implied by the term "back pressure effects." The bulk of experimental work indicates, however, that while a marked increase in arterial resistance causes a retention of blood in the left auricle, this is accommodated in the distensible pulmonary veins and does not affect the pressure curves in the arteries, provided the heart is in good condition and able to compensate in a normal manner (Straub, Gerhardt).

THE NERVOUS CONTROL OF THE PULMONARY VESSELS.

In spite of many negative results as to the effect of nerve stimulation, it can no longer be doubted that the pulmonary vessels are under the control of vasomotor nerves. This is supported by the following evidence:

(*a*) Nerve fibrils have been found in the media of the pulmonary artery (Karsner, Berkley), and more recently these have been traced directly to the muscle cells (Larsell).

(*b*) Undoubted contraction of the pulmonary artery and a decrease in pulmonary blood flow occurs after stimulation of the vagus nerve in the turtle and frog (Krogh, Carlson and Luckhardt, Mashima).

(*c*) A critical evaluation of extensive experimental work indicates clearly that epinephrin causes a constriction of the pulmonary arteries (*cf.* Wiggers for literature). To this may be added the direct observation by Hall that a constriction and complete stoppage of flow may occur after epinephrin in transilluminated lungs.

THE CARDIAC REGULATION OF THE PULMONARY CIRCULATION.

While the nervous and chemical control of the pulmonary vessels undoubtedly play an important, if not as yet fully understood, part in the distribution and flow of blood in the lungs, it is obvious that the total volume of blood contained in the pulmonary vessels must be

governed by the relative discharges of the two sides of the heart. Whenever, therefore, the systolic discharge of the right heart exceeds that of the left—as may conceivably happen either when the systemic venous inflow increases or the systemic arterial resistance is greatly raised—intense pulmonary congestion must inevitably occur unless compensatory mechanisms are set in operation.

According to Henderson, this is accomplished by an automatic cardiac regulation.

Whenever any condition increases the volume of blood pumped into the pulmonary vessels by the right heart, the rise of pressure in the pulmonary veins stimulates the left ventricle to larger strokes. So long as the left heart is capable of responding to even a moderate rise of the diastolic distending pressure by relaxation and contractions larger than any of which the right heart is capable, pulmonary congestion is effectively guarded against.

The numerous direct observations as to effects of changing systolic volumes discharged by the right heart on pulmonary pressure, lung volumes, etc., indicate clearly, however, that if such a mechanism operates in the intact circulation it is not adequate to prevent pulmonary congestion entirely. On the other hand, we must conclude that a certain degree of active pulmonary congestion and a definite increase in pulmonary arterial pressure must necessarily follow an augmented systolic discharge of the right ventricle. Indeed, it is not until the pulmonary venous pressure and blood volume are augmented in this way that the initial tension and systolic discharge of the left ventricle increase. Once set into operation, this mechanism tends to prevent pulmonary engorgement from becoming excessive, but it is never able to reduce the pulmonary volumes or pressures back to normal.

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CHAPTER IX.

THE NORMAL RESPIRATORY VARIATIONS OF ARTERIAL PRESSURE.

The observation that blood-pressure undergoes periodic variations with inspiration and expiration dates from the experiment of Stephen Hales in 1733. The relations of the pressure changes to inspiration and expiration, as well as their causes, though frequently reinvestigated, still remain a subject for research and discussion. In the following table have been gathered, after the clever manner suggested by Lewis, the findings of various observers on different animals.

Respiratory Variations in the Dog.

Year.	Investigator.	Insp.	Exp.
1860	Einbrodt	+	−
		−+	+−
1881	de Jager	−+	+−
		−	+
1882	Fredericq	−+	+−
		−	+
1908	Lewis	−	+
		−+	+−
		+	−
1910–12	Wiggers	−	+
		−+	+−

Respiratory Variations in the Rabbit.

Year.	Investigator.	Insp.	Exp.
1882	Fredericq	−	+
1882	Moreau and Lecrenier	−	+
1883	Legros and Griffé	−	+
1886	de Jager	−	+
		−+	+−
		+−	−+

Respiratory Variations in Man.

Year.	Author.	Insp.	Exp.	Method.
1855	Vierordt	−	+	Sphygmograph.
1865	Wolff	−	+	Sphygmograph.
1872	Landois	−	+	Sphygmograph.
1876	Riegel	−	+	Sphygmograph.
1877	Sommerbrodt	−	+	Sphygmograph.
1877	Klemensiewicz	+	−	Sphygmograph and respiratory tracing.
		−+	+−	
1881	Marey	−	+	Sphygmograph and respiratory tracing.
		+	−	
1881	Schweinburg	−	+	Sphygmograph and respiratory tracing.
		+	−	
1883	Legros and Griffé	−	+	Sphygmograph and respiratory tracing.
1889	Wertheimer and Meyer	−	+	Sphygmograph and respiratory tracing.
1895	Mosso	+	−	Sphygmomanometer.
1902	Mackenzie	−	+	Sphygmograph.
		+	−	
1908	Lewis	−	+	Suspended sphygmograph.
		+	−	
		−+	+−	
		+−	−+	
1910	Groedel	−	+	Uskoff sphygmomanometer.
1912	Erlanger and Festerling	−	+	Erlanger sphygmomanometer.
1914	Wiggers			
	Systolic	−−	++	Erlanger sphygmomanometer and optical registration.
	Diastolic	−+	+−	
1915	Snyder	+	−	Erlanger sphygmomanometer.
		−	+	
1922	Trotter, Edson and Gesell	−	+	Erlanger sphygmomanometer.

It is evident from this tabulation that there is no great uniformity of opinion as to the nature of the respiratory variations of pressure in different or even in the same species of animal. As Lewis has pointed out, current text-books unjustifiably present the results obtained by Einbrodt in the dog and Klemensiewicz in man. The great discrepancy is probably traceable to several factors: (1) That the mercury manometer does not always follow the changes in trend of pressure promptly, thus increasing some oscillations by resonance and making others smaller by interference of waves; (2) that these variations are due to different causes in different animals and man.

Many investigators, observing that variations in the cardiac cycle occur from beat to beat, have attributed the changes exclusively to this factor, while others have assigned the chief effect to the mechanical influence of the phases of respiration. It is more probable that both play a part.

Fredericq was probably the first to describe clearly the relative importance of each of these two factors. He pointed out that variations in blood-pressure occur in the dog during inspiration and expiration whether the heart is rhythmic or arrhythmic, with this difference: In the former case the blood-pressure falls during inspiration while in the latter it rises. He also pointed out that in animals in which no cardiac variations occur (rabbit) the pressure always falls during inspiration. He, therefore, concluded that the mechanical influence of respiration tends to reduce arterial pressure during inspiration, but that in the dog these changes are often overbalanced by an inspiratory acceleration of the heart. Inasmuch as he observed a similar variation of rhythm in his own pulse, he believed that cardiac rhythm determines the direction of human blood-pressure. This seems to be essentially correct. In the rabbit observers generally report a simple fall during inspiration and rise during expiration. In a total of ninety-seven experiments on dogs analyzed with reference to this point, the writer has found that, without exception, both systolic and diastolic pressures fall during inspiration and rise during expiration[1] as long as the successive heart cycles are of equal length. Since these variations disappear promptly during temporary apnea and reappear during the first respiratory movement, it seems safe to assert that they are caused by the mechanical influence of respiration. When marked variations in cardiac rhythm are present, however, so that the heart accelerates during inspiration, then the mean pressure rises during this phase and falls during expiration. In such cases the change in heart rate overbalances the contrary effect on arterial pressure and dominates the mean pressure curve.

Further, when the normal heart shows only a slight respiratory arrhythmia, or when the depth of inspiration and expiration is some-

[1] In these experiments the pressures were recorded in part with Hürthle membrane or spring manometers and partly by optically recording manometers.

what increased, both influences may operate consecutively, the mean pressure first declining, due to a respiratory effect, and then rising in inspiration owing to cardiac acceleration; while the mean pressure first continues to rise in expiration, due to a respiratory effect and then declines owing to the cardiac slowing. These varied effects may be briefly summarized as follows:

	Mean pressure. Insp.	Exp.
Mechanical effect alone	−	+
Cardiac effect alone	+	−
Combined effect (marked cardiac change)	+	−
Combined effect (slight cardiac effect)	− +	+ −

This, however, only imperfectly relates the pressure effects due to the heart rhythm variations, as the inference might be drawn that both systolic and diastolic pressures follow the directional change of mean pressure, which is not the case. A shortening of a cycle, as shown in Fig. 43, increases the diastolic and decreases the systolic pressure of the beat following. A lengthening of a cycle causes an elevation in the systolic pressure and a fall in the diastolic pressure of the next beat.

It seems, however, that when the mechanical effect of inspiration dominates the pressure, both systolic and diastolic pressures fall (Fig. 43), whereas, if the acceleration of the heart is predominant during inspiration the diastolic pressure rises and the systolic falls.

The results of most investigators seem to support the idea that in man a simple fall of pressure occurs in inspiration (Erlanger and Festerling, Wiggers, Snyder). This, together with the observations that in a large series of healthy individuals the rhythmic variations of heart rate are not very great, indicates that the arterial pressure is largely influenced by the mechanical action of respiration and but little by the variation in heart rate. As different polyphasic relations have often been obtained, however, it is necessary to assume that in man, too, the variations in rate may disturb the rhythm established by the mechanical influences of respiration. No attempt to separate these influences can be made unless we are capable of obtaining evidence of the variations of systolic and diastolic pressures in consecutive beats. Such qualitative variations, the writer believes, can be secured by the method proposed by Erlanger and Festerling. Applying this, the writer has found that variations in cardiac rate play some part in determining variations of systolic and diastolic pressure in man. In the minority of cases they are the dominant influence, the majority showing that the mechanical effect of respiration controls the inspiratory fall of systolic and diastolic pressures. There is, in short, no standard type of *respiratory* variation in man. The cases range from those in which respiration governs the change of pressures entirely through those in which more or less complicated mixtures of heart rate and respiratory influences intermingle to those in which extreme cardiac variations alone determine the pressure changes.

The reason that a temporary shortening of the cardiac cycle causes a fall of systolic and a rise of diastolic pressure is readily found, for while the output is decreased in systole the time of peripheral outflow from the arteries is decreased more in diastole.

Why inspiration should cause a fall of both systolic and diastolic pressures when the heart rate is constant is not entirely clear. Only two possibilities exist: (1) That the decreased negative pressure within the thorax lowers the pressures within the large intrathoracic arteries, and (2) that the output of the left ventricle is decreased. Since no absolute proof is available as to which of these two factors is concerned, a few probabilities may be weighed. If the output per beat is lessened such a change occurs in spite of the fact that the effective pressure in the left auricle is slightly increased (Wiggers). It can then only be attributed to the restraining effect of a negative pressure on the contraction of the ventricle. This seems scarcely probable, since the pressure curves of the right heart give no evidence of a decreased output during this respiratory phase (Wiggers), and the volume curves of the ventricles are not influenced by slight changes of pressure around them. With the evidence before us, it seems that the fall of pressure during inspiration is probably produced in a very simple fashion, namely, by an influence of the greater negative intrathoracic pressure on the intrathoracic arteries. Such an effect is physically possible, the old idea that the thick-walled vessels are not susceptible to pressure changes having been shown erroneous by the fact that if the aorta is tied above and below, slight variations of pressure within the closed chest are transmitted to the lumen of the artery.[1]

[1] It will be noted that this chapter contains no discussion of other factors capable of modifying the respiratory variations of blood-pressure, *e. g.*, variations in venous return, resistance or capacity changes in the pulmonary vessels, thoracic and abdominal types of breathing, rate of respiration as related to heart rate, etc. This has been purposely done because the author has not been convinced by a careful study of the available experimental work that these factors ever predominate *during normal conditions* of the circulation and respiration. That they play a large role in pathological conditions, however, may not be doubted (*cf.* also Chapter XXVII).

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SECTION II.

GRAPHIC METHODS FOR THE CLINICIAN.

CHAPTER X.

THE PRINCIPLES AND PRACTICE IN OPTICAL REGISTRATION OF MECHANICAL PULSATIONS IN MAN.

As the accurate registration of dynamic changes in the circulation can only be accomplished by apparatus of high vibration frequency, the use of apparatus writing with ponderable levers on smoked surfaces is being gradually superseded by the so-called *optical registration, i. e.*, by the registration on moving sensitive plates, films or paper through light beams of adequate intensity. Since the employment of this method in man has not only furthered our interpretation of the normal circulation but bids fair to be of value in clinical diagnosis, the details of its employment, both theoretical and practical, must be considered.

The Recording Capsules.—While a number of optically recording capsules have been designed, none equal that of the *segment capsule* devised by Frank in accord with theoretical calculations. This valuable apparatus furnishes a mechanism in which the lever (a beam of light) is without weight and its movements are not impeded or modified by friction, and which yet permits a much greater magnification than is possible in other forms of apparatus.

The principle of the apparatus is shown in Fig. 59. The recording surface consists of a circle flattened on one side so that a segment is cut off, hence the term *segment capsule*. Over the surface is stretched a thin rubber dam and on this a small trapezoidal plate of celluloid, *C*, is so cemented that its broad side pivots exactly on the chord of the circle. On this, in turn, is cemented a tiny round or square mirror, *M* (3 or 4 mm. in diameter), so that it also pivots on the chord side as an axis. On this mirror a band of light is focussed, the image of which is reflected to a sensitive plate or film (Fig. 59).

A photograph of such a segment capsule is shown in the lower left figure of Fig. 60. *S* is the capsule and *R* the mirror. In order to shift the reflected beam in a vertical as well as in a horizontal direction,

the capsule is held in a mount, *T*, resembling a miniature cannon carriage movable laterally by the thumb screw *V* and vertically by another thumb screw, *W*.[1]

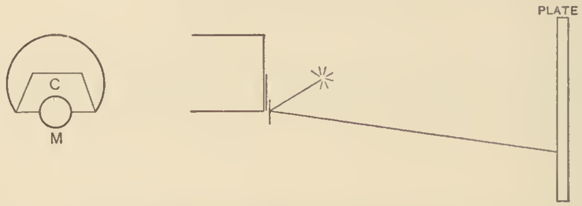

Fig. 59.—Diagram showing principle of segment capsule, mounting of mirror, *M*, and method of reflecting light beams to sensitive plates.

In order to register several dynamic events synchronously, two or three of these capsules may be vertically aligned. A convenient form of triple segment capsules has been developed for the author by Miller.[2]

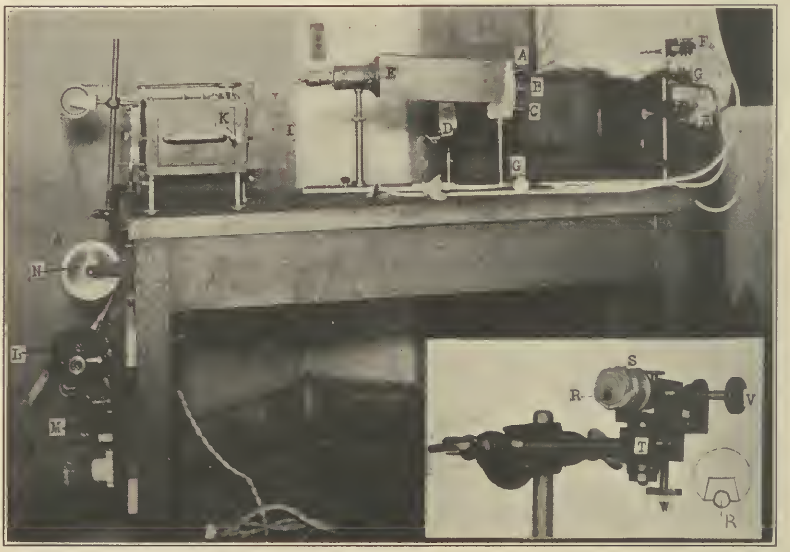

Fig. 60.—Photograph showing the mounting of Frank's segment capsules with photokymograph and light projector for hospital use. Small photograph in lower right-hand corner shows details of segment capsules.

The sensitiveness of these capsules can be adjusted to the purpose for which they are employed. For any given size it varies inversely

[1] Procurable from Eberbach & Son, Ann Arbor, Mich., or Edelmann & Son, Munich.
[2] Procurable from Eberbach & Son, Ann Arbor, Mich.

with the thickness of the rubber. For registration of pulse tracings and apex beats thin condom rubber is suitable. For registration of more delicate phenomena, such as heart sounds, Wiggers and Dean have prepared their own membranes by spreading over the surface a smooth layer of ordinary rubber cement (not vulcanizing cement) and allowing this to dry (*cf.* also heart sound capsules, page 304). The tension of the rubber is largely determined by practice. Edelmann has devised an apparatus in which the tension can be varied by a screw adjustment, but this apparatus unfortunately cannot be made absolutely air tight and, moreover, does not stretch the rubber equally. For general use a capsule 8 mm. in diameter is suggested by the author. The sensitiveness increases almost directly as the square of the radius; the larger the capsule the greater its sensitiveness. Accordingly a variety of sizes, ranging from 6 to 10 mm., meets the most exacting requirements of a research laboratory.

As the sensitiveness depends, to a considerable degree, on the size and position of the plate, care should be taken that such instruments are carefully constructed and attention should be paid to the placement of the mirror plate. Since the sensitiveness decreases as the plate approaches the center or reaches beyond it, care must be taken that it is always placed peripheral to the center of the capsule. The relation of the cord to the circle modifies the sensitiveness as well; the smaller the arc subtended by the chord the greater the sensitiveness. Thus, a chord side with an angle of 60 degrees is less sensitive than one with 45 degrees. Mathematically, the sensitiveness is expressed by the formula $\gamma = \frac{r \cdot \varphi}{S}$, where r is the radius, S the tension and φ a factor allowing for the form and position of the plate (Frank).[1] For general use the author suggests a capsule in which the chord subtends an angle of 45 degrees.

The Projection System.—In initiating work in optical registration, Frank devised a convenient projection system shown in Fig. 60. A vertical glowing Nernst lamp filament included in a housing, *E*, is directly focussed by three lenses, *A*, *B*, *C*, on three capsules vertically aligned *with their chord side down*. From each mirror a vertical band of light, which is really the image of the glowing filament, is projected on a photokymograph in which the paper or plate moves horizontally. Just in front of the Nernst filament the pendulum of a clock, *D*, regularly interrupts the beams and records directly on the curves, thus marking 0.5-second intervals (*cf.* Fig. 69). The light intensity is sufficient to record at distances of about 1 meter. The chief drawback consists in the fact that the width of the reflecting light band is not variable. Bands of different width are, however, desirable in order to obtain clear-cut records. In general, the recording band should

[1] For further details, *cf.* Frank: Ztschr. f. Biol., 1908, **50**, 342.

be the broader the larger the amplitude of the excursion. If records of large amplitudes are taken with too narrow a band the sharp upstrokes do not record at all or only faintly, owing to a lack of actinic action. Inspection of such records as are shown in Fig. 69 indicate that as the light band moves up rapidly the lines thin out. This difference from the appearance of drum tracings is due to the fact that the latter are written by a point while the optical tracings are recorded by a vertical line of light, for as the long beam falls across the camera slot a line of light as wide as the band is focussed by the camera lens on the sensitive surface. If the light band is stationary while the paper moves a broad line is traced; if, however, the band moves the line thins out in proportion to the velocity of movement. If the amplitude of excursion is small, details are often much more clearly indicated when the light band is narrowed (*cf.* Fig. 64, *B*, *C*, *D*). To

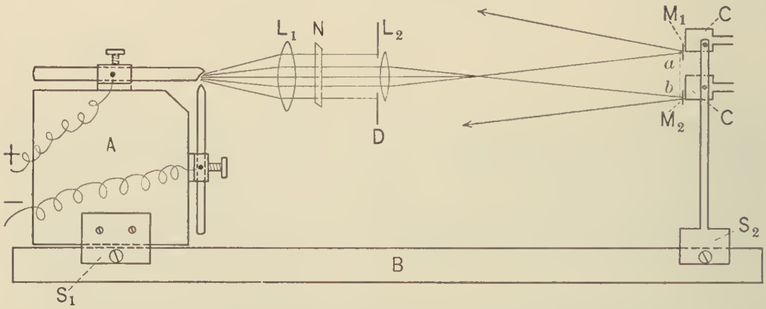

FIG. 61.—Diagram of optical illuminating system for reflecting light from segment capsules. *A*, arc light, movable on a solid bench, *B*. Rays from positive carbon pass through a condensing lens, L_1, and an adjustable slot, *N*, the image of which is focussed by a lens, L_2, and projected upon the mirrors, M_1 and M_2, of the segment capsules, *C*. These capsules are supported on a vertical rod sliding by a clamp, S_2, upon bench, *B*.

accomplish this the author has devised a small carbon projecting lamp in which an adjustable vertical slot is illuminated and its image is then thrown on the mirror by a projecting lens. The details are shown diagrammatically in Fig. 61, and an illustration of the lamp may be found in an earlier publication.[1]

This arrangement has the disadvantage, however, that only a single frontal lens may be used and consequently only a single beam of light can be projected. With the disappearance of the Nernst lamp from the American market we are at present forced to this mode of illumination, as no other satisfactory substitute has as yet been found. Such a single light beam may, however, be projected on two capsules arranged in line with the beam, or by skilful manipulation and use of the triple segment capsule above referred to, on three at

[1] *Cf.* Arch. Int. Med., 1915, **15**, 77.

one time. In the case of a horizontally moving paper a horizontal beam of light may be focussed on several capsules arranged side by side *with their chord side down.* In the case of a vertically moving paper the slot is rotated so that a vertical beam of light is projected on three capsules vertically arranged *with their chord side turned to the operator's right.* A convenient arrangement of such a multiple capsule system on a bench, as shown diagrammatically in Fig. 61, permits the entire outfit to be placed on a table extension in front of a string galvanometer and thus makes it possible to obtain mechanical records simultaneously with the electrocardiogram.

The Recording Camera or Photokymograph.—The principles and details involved in the construction of photokymographs cannot be entered into at this place. Any form of camera suitable for electrocardiographic work may, however, be employed.[1]

The choice of recording material is largely a matter of individual preference. The author prefers bromide paper especially for these types of registration for the following reasons: (1) Ease in handling and development; (2) cheapness; (3) the reproduction of a black record on a white surface; (4) the absence of light reflection common in more sensitive surfaces, and (5) ease in duplication of any section by photographing on "process" plates and reproducing as prints.

Alignment of Apparatus, Parallax.—In establishing precise time relations between two or more simultaneously recorded tracings, account must be taken of possible errors due to parallax. It is well known in physical optics that in order to have the registering beams focussed in the same plane it is essential that the middle of the various reflecting mirrors be mounted in the same plane as the cylindrical lens of the photokymograph. If this is not done and the light beams strike the camera lens at slightly different angles they are focussed as lines which are not absolutely over one another.

It is obvious that in the arrangement above referred to such an alignment of capsules is not feasible, that the different surfaces are not arranged in the same plane as the cylindrical lens, but, on the contrary, at right angles to it. Actual tests have shown, however, that, in the mounting above referred to, the error of alignment due to parallax is so small that it may be disregarded in time determinations in which the paper does not move more than 80 mm. per second. By means of a deep and narrow hood in front of the camera the author has minimized such errors, for when the alignment is such that variations greater than 0.75 mm. occur, no record can be obtained. Various

[1] Plate camera may be obtained from the Cambridge Scientific Instrument Company, Cambridge, England. Cameras adapted for vertically moving papers or film may be obtained from the Hindle Company, Ossining, New York, Cambridge Scientific Apparatus Company, England, or Edelmann & Son, Munich. Upright cameras of special design have been devised by Frank, Garten and the writer, but these are not on the market. Upright cameras retaining the essential features of vertically recording cameras will probably be constructed to order by either the Hindle or Edelmann Company.

methods have been suggested for taking into account errors due to parallax (Garten, Frank, C. Tigerstedt, Straub). In the Nernst light arrangement of Frank, where a pendulum regularly interrupts the same portion of the light beams, synchronous points may readily be established on different curves. A similar arrangement cannot be employed, however, with an arc light, in which different sections of an illuminated slot are thrown on different mirrors. When great accuracy is required corrections may, however, be readily made for differences of alignment by photographing the quiet beams on stationery paper through a piece of amber glass, a procedure suggested by Garten.

Time Records.—Time intervals may be recorded in a variety of ways. When the apparatus is used in connection with a string galvanometer the projection of time lines by the rotating motor offers the simplest and a very satisfactory time projection. When the apparatus is used by itself other forms of time record are necessary. The simplest procedure consists in photographing the shadows of pointers mounted directly in front of the camera lens. Either a Jaquet time signal giving one-fifth second, or a tuning fork vibrating fifty times per minute or any form of electrically operated signal may be used. As a source of light, a small circle or band of light emanating either from a separate projecting system or from the same source and reflected from a vertical mirror may be thrown on these time recorders. A small stereopticon with nitrogen bulb, in which the slide holder is replaced by an iris diaphragm, has been found very useful by the writer. Frank has introduced a swinging pendulum in front of the light which directly intersects the light band. Feil and Gilder similarly interrupted a separate beam of light at its focus by a rotating interrupter.

Minor Details.—Success in registration is often thwarted by inattention to apparently minor details. Owing to light diffraction and the consequent development of photoinactive rays at the margin of bands, the edges of records may become furred or irregular when the size of the mirrors is too small in relation to the camera distance. With mirrors as small as 2 mm. in diameter, however, excellent records may be obtained provided the camera distance is not greater than 150 cm. and the light is accurately focussed on a single mirror. When several mirrors are used it is advisable not to have the camera more than 120 cm. away.

In order to insure good results the small mirrors should have a good reflecting surface. Absolutely plane first-surface mirrors, while theoretically desirable, are difficult to obtain and even more difficult to keep bright. The author has found that silvered No. 1 cover-glasses, cut into small squares by means of a diamond point, are quite sufficient for all purposes. Owing to their cheapness they may be frequently renewed. These tiny mirrors should be cleaned, benzol being preferable, as they are often soiled with rubber cement. They are most readily handled by a small pair of flat-nosed pliers.

Before using the apparatus it is desirable to ascertain that it is air tight for small positive and negative pressures. If the capsules are connected to receiving apparatus by tubing of approximately the same length, any error due to air transmission may be ignored; for extreme accuracy it can, of course, readily be determined. As to the choice of registering surfaces the following information may be added: As the intensity of light is sufficient, relatively "slow" plates should be selected for most purposes. So-called "process plates" or "film," on account of their definition, are suitable. For films, so-called "positive film," now used in the moving-picture industry, is preferable. For paper registration, rapid bromide papers, such as Eastman P. M. C. or Defender Monox, are most suitable, although for slow-speed work, "chloride papers" may be used to advantage.

It seems scarcely necessary in these days of general photographic knowledge to give details as to developers, fixatives, etc. The mode of development is also a matter of individual taste. Even when considerable volumes of paper records have to be handled the author still favors simple ocular inspection in preference to factorial development. It is really simpler, less time-consuming and gives better results. For films requiring longer time for development, tank development is preferable.

Determination of Inherent Vibration Frequency.—Damping and Sensitiveness of Apparatus.—While the capsules fitted as above described may be considered to have a vibration frequency adequate to record pulse and volume curves for man, it is often desirable, for special reasons, to be quite certain that the capsules have an inherent frequency in excess of that of the most rapid vibrations to be recorded. As it is quite obvious, to judge from vibration frequencies quoted in the literature, that many investigators are still unfamiliar with the way in which such frequencies are determined, the methods and principles of determining may be briefly stated. Before doing so it is desirable, however, to digress for a moment and consider briefly the physics of vibrating membranes. Every freely swinging membrane if suddenly set in motion continues to vibrate with gradually diminishing amplitude (Fig. 62, *A*) before coming to rest. Such a membrane is called *periodic* and the vibrations are spoken of as the *inherent* or *free* vibrations. The time consumed by each vibration is called the *inherent vibration period* (often designated by T), while the number of vibrations it would execute in a second is the *vibration frequency* of a membrane (often designated by N). It is obvious that the frequency is the reciprocal of the period ($N = \frac{1}{T}$). Hence, we say synonymously that an instrument has a short period or a high frequency. The number of vibrations taking place before complete rest occurs depends on the friction due to damping. If damping is slight each successive vibration is only slightly diminished in amplitude and a considerable number of free vibrations result (Fig. 62, *A*). On the other hand, if damping is

moderately great only a few after-vibrations take place before rest occurs (Fig. 62, *B*). The rate of reduction in amplitude is called the *vibration decrement.* If damping is great enough to prevent all free vibrations the apparatus is called *aperiodic* (Fig. 62, *C*).

Every membrane that has its own tendency to swing may follow imparted vibrations, such as extraneous vibrations of any kind. It is obvious that no membrane can follow vibrations having a frequency

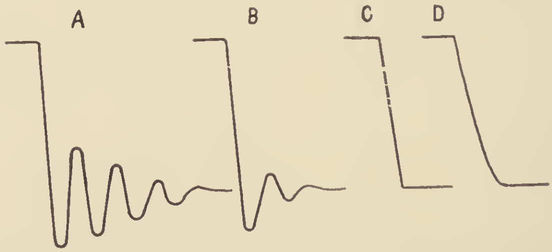

Fig. 62.—Diagram showing the behavior of a membrane under different damping conditions when a strain is suddenly released. *A*, undamped membrane; *B*, partially damped membrane; *C*, ideally damped membrane; *D*, over-damped membrane.

greater than the inherent period of the instrument. It reacts with maximum vibrations to waves having the same frequency as the membrane itself, a phenomenon called *resonance.* If a miscellaneous series of waves, equal in amplitude but differing in their periods, are recorded by a membrane whose period is equal to that of some of these waves, but is greater or less than that of others, their amplitudes will not be recorded correctly. As shown schematically in Fig. 63, the

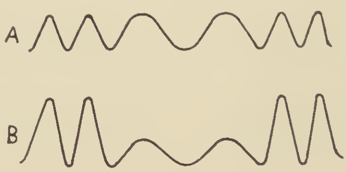

Fig. 63.—Diagram to show the influence of resonance in reproducing sound vibrations. *A*, a theoretical series of vibrations of equal amplitude but varying periods; *B*, record of same by membrane having an inherent period corresponding to the first and last waves.

vibrations with periods closely approximating that of the apparatus will appear larger than those occurring at a rate which is either faster or slower. In recording, therefore, it is necessary to employ a membrane with a period not only as short as but very much less than the shortest oscillation to be recorded.

It is possible for the damping of a membrane to be excessive. When this occurs the membrane is prevented from following the rate of the

imparted vibrations accurately; hence, not only is their contour altered but their amplitude is unduly diminished. On the other hand, if a membrane is not aperiodic it has a tendency to add its own vibrations to the imparted vibrations. When it is difficult to produce an optimum damping it is more rational to err slightly toward a periodic system and maintain the apparatus only approximately aperiodic, provided always that the apparatus has an inherent vibration rate well in excess of the oscillations that it records.

The vibration frequency may be determined in several ways. In the method devised by Frank the capsule is connected by tubing with a thistle tube or a receiving tambour covered by the thinnest rubber dam, which is drawn over its edges *as tensely as possible.* A positive pressure is then created within the system through a side opening. When all is ready to make the test and the photokymograph is running the pressure is suddenly released by puncturing this stretched rubber membrane either by means of a hot rod or an electric spark. Such records are illustrated in Fig. 64, *E* and *F*.

A second method suggested by Van Zwaluwenburg and Agnew utilizes the principle of resonance. By singing a scale of notes in an even voice into the mouth-piece, a series of vibrations for each note can be recorded photographically. Their amplitude will vary, for the membrane responds with the maximal vibrations to the note having the same frequency as its own. The difficulty consists in singing sounds of equal intensity. If the loudness of the singing voice changes the amplitude will necessarily vary in proportion.

The decrement of the inherent vibrations depends on the degree of damping. In the Frank capsules no special mechanism for damping exists, but it is unnecessary and, in fact, undesirable, as has been experimentally determined. When it is necessary to record tachograms or heart sounds the damping of the air column is materially affected by the relative size of the side opening. The determination of the decrement of such an open system requires special procedures to draw the membrane out of equilibrium. This cannot be carried out satisfactorily without difficulty. A tiny steel splinter may be centrally supported on the membrane and the membrane deflected by an electromagnet, or a light string may be included in the membrane at the time of its manufacture by which the membrane is drawn out. By suddenly demagnetizing the coil in the first instance, or by quickly severing the string, the membrane is thrown into a few oscillations. The relative decrease in succeeding vibrations should be great and not more than two or three vibrations should occur. As a rule, an apparatus may be regarded as approximately aperiodic without this special test when the vibrations of the closed system decrease rapidly in amplitude, as shown in Fig. 64, *E* and *F*.

The sensitiveness of the system may be determined by connecting to the rubber tube of the closed system a U-shaped water manometer

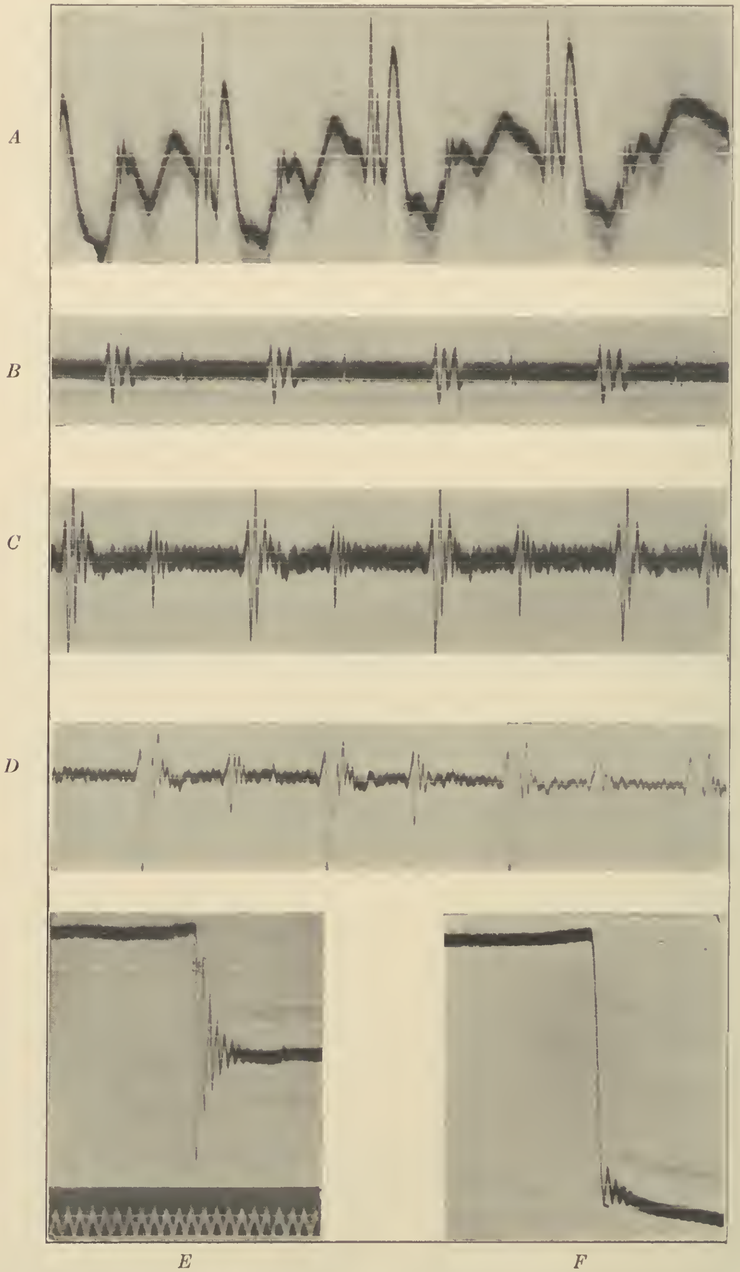

FIG. 64.—*A*, apex curve taken with subject in sitting posture; *B*, curve recorded with same apparatus but side tube open; *C*, record from same subject taken by our modified capsules; *D*, more satisfactory record of same, due to use of narrower band of light; *E*, curve showing the method of determining the vibration frequency; *F*, curve showing the damping influence of an open side tube.

in which the pressure can be varied slightly by a piece of closed rubber tubing attached to one limb. The excursion of the beam of light when 1 mm. of water pressure exists in the closed system may be read on the centimeter scale of the camera.

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CHAPTER XI.

THE ARTERIAL PULSE.

Definition.—By the *pulse* we mean the expansion and elongation of the arterial walls which are passively produced by variations of intra-arterial pressure during systole and diastole. As already analyzed (*cf.* page 144), no active contraction of the arterial muscle is involved. When blood is suddenly thrown into the aorta during systole it is accommodated partly by moving the entire arterial column onward at a greater velocity, but largely by distending the arterial wall under the pressure generated by the ventricle. As this increase in pressure is transmitted toward the periphery, the arterial distention is also communicated from one segment of an artery to the next peripheral segment in the form of a wave, the velocity of which is entirely independent of the velocity of the blood flow. This is evident from the fact that the pulse wave is transmitted peripherally at a velocity of some 6 to 10 meters per second, while the average velocity of the blood flow is probably about $\frac{3}{10}$ meter per second. The relation of the pulse wave and the blood flow may be compared to an impact transmitted through a train of cars in motion; the rate at which the impact travels is entirely independent of the speed of the train, and may, in fact, occur in an opposite direction.

METHODS OF RECORDING THE PULSE.

The methods devised for registering the pulse in various regions may be reviewed according to the principles upon which they are built.

Wrist Sphygmographs.—A sphygmograph is an instrument in which a button is pressed on the skin over an artery by a spring, its movements being communicated by a lever system to moving paper. It is apparent that in principle the sphygmograph is a tension recording device and comparable to a spring manometer, the elastic arterial wall corresponding to the membrane.

Patterns of Wrist Sphygmographs.—The first sphygmograph utilizing a spring was that devised by Marey (1857–1860). In this instrument the movements communicated to the spring are recorded by a simple lever. Von Frey subsequently improved upon this type of sphygmograph by a better construction of the lever. It remained for Dudgeon to enhance the compactness of the instrument as well as its sensitiveness by supplanting the simple with a compound lever which writes without an arc on a horizontal surface. The subsequent instrument of

Jaquet, based on the same principle, was a practical advance in the sense that the instrument is more firmly supported on the wrist and has a very good time marker.

The flat spring remained in use until Frank and Petter (1908) devised their sphygmograph (Fig. 65). In this apparatus the button *p* is pressed upon the artery by a spiral spring, *o*, which is applied near the axis of the lever *l*. The tension of the spring, and hence the pressure of the button, can be regulated by the screw *h*. The movement of the button is transmitted to a double lever, *b c*. The arm *b* pivots on needle points, but the arm *c*, which is held in fixed conical bearings, is equipped with a spiral spring under slight tension so directed that it pulls the lever forward as soon as the button moves up. The paper moves on a plate curved to counteract the arcs written by the lever *c*.[1]

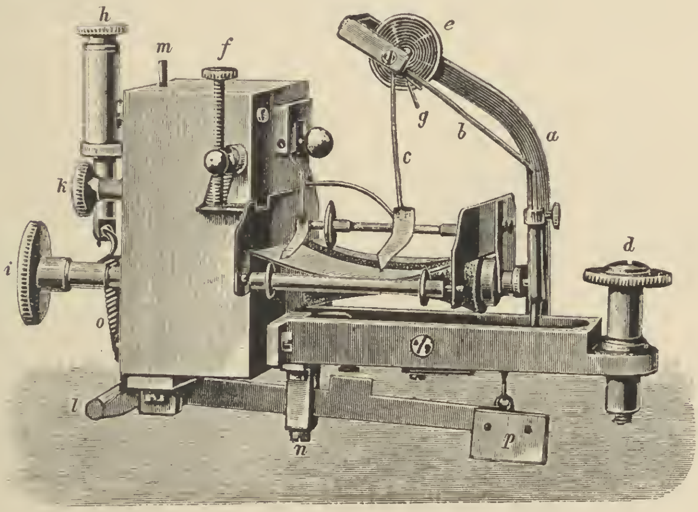

FIG. 65.—Perspective view of Frank-Petter's sphygmograph.

In 1910, Jaquet entirely rebuilt his sphygmograph, utilizing all the essential ideas of the Frank-Petter apparatus, except that the old lever system in fixed bearings and the straight paper lead were retained. In describing tracings it is, therefore, desirable to designate whether they were taken with the old or the new form of Jaquet sphygmograph, so that their value may be correctly estimated (*cf.* Fig. 73).

Critique of Wrist Sphygmographs.—Since the sphygmograph is based upon the same principle as the spring manometer, it is possible to analyze its efficiency upon the same basis. The ability with which

[1] The Frank-Petter and Jaquet sphygmographs may be obtained through M. Schaerer, Bern, Switzerland. The Jaquet sphygmograph is also supplied by A. Thomas Co., Philadelphia, and by Zimmermann, Leipzig, Germany.

it accurately follows the pressure variations is determined by its inherent vibration period T, or its frequency $N = 1/T$, and by its damping, which may be estimated from the logarithmic decrement of the vibrations. The periodicity is determined by the formula $T = 2\pi\sqrt{\frac{m'}{E' + e}}$, in which m' equals the calculated effective mass E', the elasticity coefficient of the spring and e, that of the tissues and artery. The efficiency of an apparatus depends not only upon its inherent vibration rate, however, but also upon the magnitude with which the pressure changes are reproduced. Frank has, therefore, expressed the efficiency by the formula $G = \epsilon N^2$, where ϵ represents the sensitiveness of the writing point and N the vibration frequency.

By applying the theoretical formulæ evolved, Petter was able to determine the relative value of the different instruments. The figures shown in the following table, extracted from a more complete compilation by Petter, show that in none of the sphygmographs constructed upon experimental principles does the vibration rate reach the required level of 32 per minute (Frank). It is further of interest to note that, with the exception of von Frey's, each successive model of the sphygmograph following Marey's, in becoming more convenient for practical use, has decreased in efficiency. The Frank-Petter apparatus alone seems to have the required vibration frequency. Its efficiency, as compared with the Jaquet (old form) is as 3000:150. These facts are indicated in the following table:

Apparatus.	Efficiency, G in 10^{-5}.	Vibration, N.	Damping constant, K in 10^3.	Magnification of lever.
Marey (first model) . .	300	13.0	6–20	50
von Frey	360	11.0	9–35	90
Dudgeon	150	9.2	4–20	50
Jaquet (old)	150	7.0	35–100	100–140
Frank-Petter	3000	32.0	0.5–3	50

The records obtained with all instruments except the Frank-Petter model, therefore, require correction. The distortion produced by different instruments was also investigated by Petter through the use of artificial pulses of known form. Thus, the curves recorded by the Dudgeon apparatus (Fig. 66, *A*) and the curve of known form rose almost simultaneously from the base line and returned practically together. For time determinations the Dudgeon would, therefore, be sufficiently exact were it equipped with a time recorder. Neither the height nor the contour, however, are correctly reproduced. The dicrotic notch appears relatively too low and the elevation begins too late. This is due to the fact that its vibration period is low and its damping very slight. It is evident that the Dudgeon apparatus is not reliable in giving the correct shape of the radial pulse.

The records obtained with Jaquet's apparatus (old model) are even

worse (Fig. 66, *B*). No true pulse curves are recorded. The rise and return to the base line are delayed; the rise is steeper and exceeds the true height. The dicrotic wave is not recorded at all but is replaced by a series of after-vibrations, which have deceived investigators since the instrumental period happens to correspond closely to that of the dicrotic wave.

In testing the Frank-Petter apparatus the curves were found to differ only in that a few inherent vibrations were present in the upstroke.

There is, however, a simpler and more practical way of testing the efficiency of an instrument which every user of an apparatus can readily apply. This procedure, the introduction of which we owe to von Frey, consists in recording pulse tracings with different pressures of the button. If the apparatus reproduces the pulse curve accurately only the amplitude and not the contour of the curve will alter, whereas if this is not the case the curve will have a different form

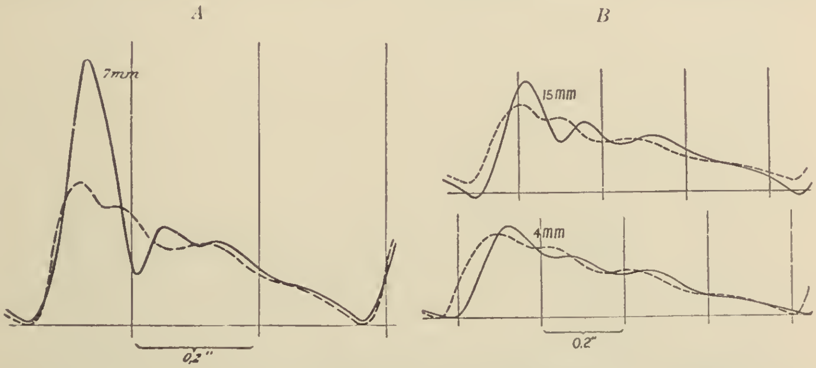

Fig. 66.—Experimental tests of the efficiency of sphygmographs. *A*, Dudgeon record; *B*, Jaquet record compared with true curves (broken line). (After Petter.)

with every pressure. The latter, it is almost universally recognized, is the case with the instruments in common use. The writer has applied von Frey's criterion to the new form of Jaquet. In the case of this instrument it is found that the degree of pressure affects the character of the pulse form. This, in agreement with the findings of Veiel and Noltenius, indicates that by incorporating the old form of fixed axis bearings and a different style of lever the efficiency of the instrument still remains low.

Technic of Taking Sphygmograms.—Owing to the fact that pulse curves of different form, as well as amplitude, have been obtained by different pressures of inadequate sphygmographs, it has frequently been debated at what pressure the most correct curves are obtained. From what has preceded, it is evident that the shape and contour of curves recorded with an accurate instrument do not change with varying pressure. Ohm has succeeded in recording true curves with-

out any pressure by cementing a small mirror over the radial artery. Those forms of sphygmographs, the vibration frequencies of which are too low, do not correctly reproduce the oscillations under any pressure. Therefore, the only question of interest is, At what pressure are the records most nearly correct in contour? It is generally believed that the button applied to the artery follows the pressure variations best when the intra- and extra-arterial pressures approximate each other. It is during such pressure relations that the largest oscillations occur, hence it is generally assumed that the greatest amplitude of oscillation is accompanied by the curve of most correct form. This, however, is fallacious, since, as the excursions become larger, the incidence of lever throw and inherent oscillations become greater and the deviation from the correct curve more pronounced. This is clearly shown in the two tracings of Fig. 66, *B*, in the upper curve of which the amplitude of the original record was 15 mm. and that of the lower 4 mm. The truer form is given when the records are of smaller amplitude. Taking curves of larger amplitude is, therefore, not to be encouraged with instruments of low vibration frequency.

The question as to the proper tension of the sphygmograph band has also come up for discussion among investigators. Thus, Hirschmann pointed out the danger from venous stasis if the band is too tight. Mackenzie believes that the use of the rigid fixation for a sphygmograph is entirely wrong in principle and has used instead an elastic band. Lewis has sought to obviate the defect of the ordinary sphygmograph by substituting for it a suspended sphygmograph. The reason for selecting such a fixation lies in the fear that the varying filling of the venæ comites may affect the pulse curve (Hirschmann, Hill, Barnard and Sequeira, Lewis). It is questionable, in view of the work of Frank and Petter, whether the variation in the venous volume plays any role in determining the form of the curve. However this may be in the rigid fixation, the elastic fixation or suspended application has the decided drawback that the body of the apparatus itself may be set in motion and add to the extraneous oscillations. It is, in fact, theoretically desirable, as Petter emphasizes, to adjust the apparatus so that the body is absolutely rigid as compared to the artery beneath. According to Petter, even the elasticity of the ordinary bands of some forms of sphygmographs adds materially to their inaccuracy.

Transmission Sphygmographs.—In the transmission sphygmograph (Fig. 67) the movement of a spring and button similar to those of the direct sphygmograph is communicated to a larger tambour covered with rubber, and the compression of the air thus produced is communicated to a second tambour patterned more or less after the well-known form of Marey. Marey, Grunmach, Knoll, Edgren and Mackenzie have employed apparatus of this kind. The practical advantage consists in the fact that the pulsations can be recorded simultaneously with other pulsations and that it is adapted to determine the velocity of the pulse waves.

No scientific critique of these forms of apparatus has been evolved. It may be said, however, that with the best possible construction a transmission apparatus is less efficient than one with direct lever transmission. The inertia of the recording tambours is the chief drawback. In the Mackenzie polygraph, the lever of which is armed with an ink pen, the tambour and lever have a vibration frequency of 4.5 per second. In the tambour supplied with the portable polygraph of Zimmermann the inherent frequency was found to be 5.8 per second. In the Jaquet polygraph the vibration frequency is 6.5 per second. (Personal tests.)

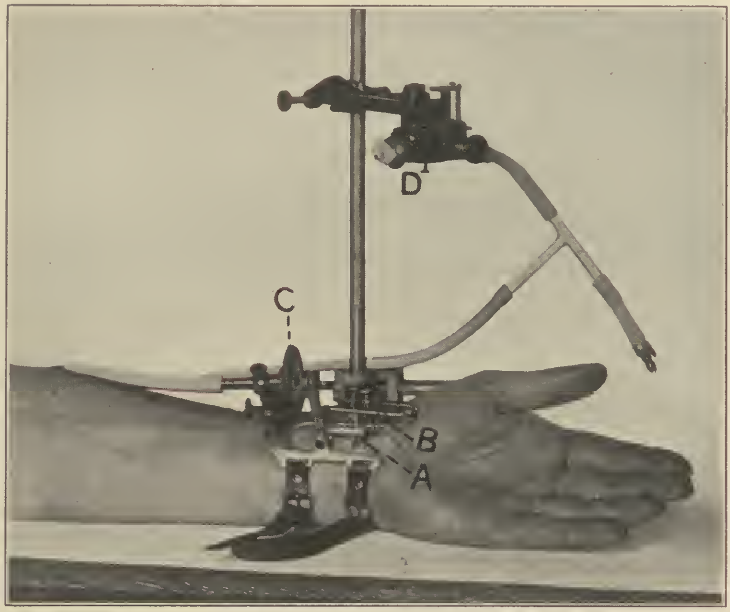

FIG. 67.—Radial transmission sphygmograph and Frank's segment capsule.

Optical Transmission Sphygmographs.—To improve the efficiency of this form of sphygmograph, Frank substituted a segment capsule (see page 179) for the recording mechanism. With this is connected a piece of soft rubber tubing tied on one end and fastened over the artery by a pressure clamp. By this apparatus the nature of the pulsation is reproduced in trustworthy fashion.

The writer has found the sphygmograph shown in Fig. 67 very satisfactory. A small button, *A*, attached to an L-shaped lever is pressed upon the radial by an adjustable spiral spring, *B*. The lever works in free axes, being held by the spring very much as in the Frank-Petter sphygmograph. As the button rises, the movements are transmitted to a capsule, *C*, covered with very light rubber and communicat-

ing with a segment capsule, *D*. It has the advantage over the method proposed by Frank that the pulsation is obtained from a single spot and that a definite tension can be employed.

The technical difficulty existed in this as in all other known forms of sphygmograph in that a rigid support of the apparatus is not available. In fact, the basal framework of all instruments seems to have been constructed as though the radial artery ran in the middle of the forearm and wrist. Consequently, when a top-heavy wrist-sphygmograph with such a support is strapped on, it tends to swing inward and outward, seesawing on its base over the outer edge of the radius.

To obviate this difficulty of fixation and retain all the advantages of a construction based on the Frank-Petter principles, Baker and the author devised a new form of transmission-sphygmograph which, when used in connection with optical recording capsules, reproduces unvarying pulse contours at different spring tensions and is, therefore, adequate for registering the contour of the peripheral pulse with accuracy. It may also be used with polygraphs of various designs, but it should be emphatically stated that the accuracy of the reproduced pulses then depends on the quality of the particular recording tambour.

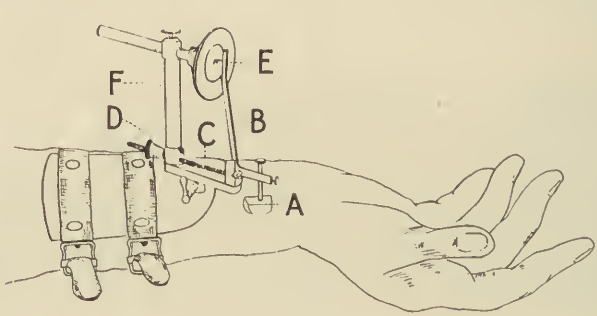

Fig. 68.—Radial transmission sphygmograph for use with optical capsule. *A*, button pressed upon radial artery by spring, *C*, operated by thumb screw, *B; D*, lever arm transmitting pulsations to tambour, *B*, which is connected with optical registering capsule. (After Wiggers and Baker.)

The details of the apparatus are shown in Fig. 68. Fixation is obtained by fastening to the lower forearm a median plate fitted to conform to the contour of the arm. The sphygmographic portion consists of a button, *A*, an L-shaped lever, *B*, pivoting on steel points, a spring, *C*, for adjusting its tension by a convenient knob, *D*, and a receiving tambour, *E*, in contact with the upright limb of the L-shaped lever. All of this portion is rigidly mounted and can be rotated on an upright rod, *F*, fastened to the median plate. Used on the left arm, the button and vertical lever are swung to the left; used on the right arm, they are swung to the right, as shown in Fig. 68. This swing has

the further advantage that the radial artery may be palpated during the process of adjustment and assurance obtained that the button is actually over the artery.

The following dimensions of parts may be added: Median supporting plate, length = 9 cm.; width = 5 cm. above, tapering to 4 cm. distally. Vertical arm of lever = 5.5 cm.; horizontal arm, 1 cm.; magnification, 5 ×. Variation of spring tension, counterbalanced by 50 to 250 gm. placed on button. Diameter of receiving tambour, 4.5 cm.; diameter of plate, 2.3 cm.

This list by no means includes all the tension devices described for recording the radial pulse. Their number is legion. The attempt has here been made to present only those instruments which are in common use or the employment of which is likely to be considered in practical work. At the end of the bibliography is given a partial list of references dealing with some of the rarer forms of pulse instruments not considered in this volume.

Volumetric Pulse Registration.—In contrast to the methods which register the pressure variations in the artery are those which measure the volume changes of the arterial wall during systole and diastole. Theoretically, such apparatus should be so adapted that its application causes no changes in the oscillations.

Cup-tambour Method.—When an open cup is firmly pressed to the skin over an artery, such as the carotid or subclavian, and connected to a recording tambour, a pulse wave is obtained which represents the expansion of the artery below. This method is commonly employed in polygraphic work. In determining the transmission time of the pulse it is often combined with the radial transmission sphygmograph. It is applicable to the subclavian, carotid and temporal arteries. Since the accuracy of the method depends largely upon the recording tambour, and since the vibration period of the ordinary tambour is inadequate to record central pulse details, a segment capsule has been substituted for the tambour by various workers. By this apparatus, Frank, Friberger, Veiel and the writer have obtained pulsations from the subclavian artery, which reduplicate all the details obtained from the aorta by optical manometers, thus incidentally establishing the adequacy of the apparatus (Fig. 69).

Finger Plethysmograph.—If a finger is inserted through a properly fitting rubber cuff into a small glass tube, and this in turn is connected to a delicate tambour, piston recorder or preferably an optical recording capsule, an expansion curve of all the arteries thus enclosed may be readily obtained.

Sphygmoscopic Pulse Tracings.—The sphygmoscope is a device in which a high oscillatory pressure is prevented from acting upon a delicate membrane by interposing a heavy membrane or ball, enclosing this in a chamber and allowing its pulsations to be transmitted to the

recording tambour. The arm-bag, rubber ball and tambour of the Erlanger and Uskoff apparatus (see page 340) represent such a sphygmoscope system.

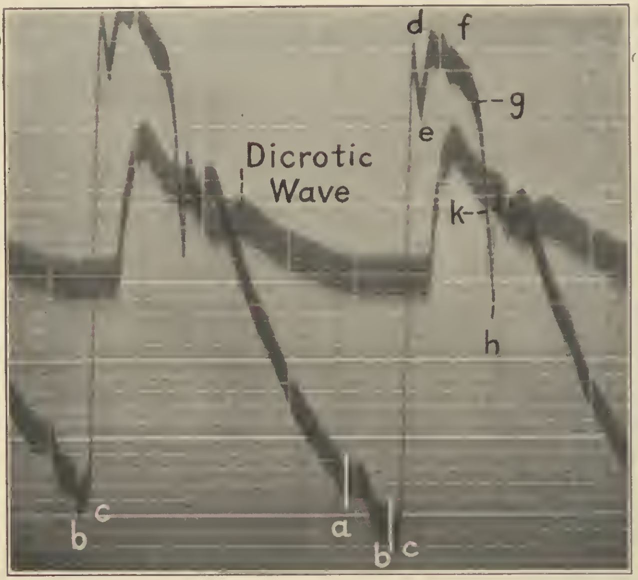

FIG. 69.—Tracing showing the difference between the subclavian (central) and radial (peripheral) pulse in man. The delay of the radial is well shown.

Sphygmomanometer Pulse Tracings.—Tracings are frequently taken, especially in polygraphic work, from the brachial artery by applying a cuff of an Erlanger sphygmomanometer or an Uskoff sphygmotonograph, inflating it by a variable pressure and recording the pulse so obtained. The shape of the curve varies with the external pressures and consequently cannot be considered to be accurate at any pressure (*cf.* Fig. 124). Their principle of construction is opposed to their yielding at any pressure an accurate picture of the pulse form. Therefore, the method cannot be used for determining the contour of pulse tracings, but may be of value in roughly establishing time relations.

The Hot-wire Sphygmograph.—Recently, A. V. Hill has designed an apparatus in which the puffs of air created in a transmission system are blown upon a heated wire. As the resistance of the wire varies with the temperature, the changes in electrical current thus induced may be recorded by a string galvanometer provided the wire is made one of the arms of a Wheatstone bridge. A little consideration of its construction as well as Hill's own records indicate that *this is not a sphygmograph* in the sense that it records pressure variations in an artery, but belongs rather to the tachographs. Probably a differ-

ential curve of both volume and pressure changes is actually recorded, and, as Hill himself points out, the apparatus is serviceable only in calculation of time relations.

The Central Arterial Pulse and its Conversion into the Peripheral Arterial Pulse.—If a receiving cup[1] be firmly pressed into the supraclavicular fossa (so as to prevent registration of venous volume changes) and connected by a closed system to a segment capsule, the optically recorded curves show all the essential details already described as characteristic for the aortic pressure curve (Figs. 22 and 23). The *central pulse*, as the pulse in the large arteries near the heart is called, shows (Fig. 69) first two preliminary vibrations: One due to auricular systole, *a–b*, the other to the isometric rise of tension in the ventricle *b–c*. These are followed by a sharp primary oscillation, *c*, *d*, *e*, 0.013 to 0.02 in duration and beginning at the ejection of blood into the aorta. It is due to the fact that the sudden ejection has set the arterial column in vibration. After this vibration the arterial curve follows the intraventricular pressure, for now ventricles and arteries are a common cavity. First, the pressure rises, *e*, *f*, thereafter reaches a more or less definite summit and then falls gradually during the rest of systole, *f*, *g*. At the beginning of the ventricular relaxation (diastole) there is a rapid backward movement of the blood toward the heart, causing the pressure to fall suddenly, thus creating the *incisura* of the central pulse, *g*, *h*. Several after-vibrations of the valves and blood column, *k*, recognized over the chest as heart sounds, follow. The pressure then falls smoothly except for a few slight oscillations due, no doubt, to reflections from the peripheral bifurcations of arteries (Frank).

These complicated series of pressure variations present in the aorta and large arteries are modified in their peripheral transmission by *friction* and *interference with reflected waves* (Frank). Or, one may state the case differently by saying that the vascular system represents a manometer system, the ability of which to transmit the pressure variations in the central arteries faithfully to the periphery becomes less and less as the length of the column increases (Weber).

The changes actually noted as we pass, step by step, to the peripheral vessels are: The preliminary and primary oscillations are damped and obliterated, the sharpness of the incisura is reduced and finally replaced by a rounded *dicrotic* dip and elevation; the upstroke is delayed and becomes more gradual, the tops are more rounded and the amplitude smaller until in the smallest arteries and capillaries the pulse is entirely obliterated. These changes in the pulse in its transmission from the subclavian to the radial artery are well shown in Fig. 69.

The part that reflected waves play in the production of the *dicrotic notch and wave* in the peripheral pulse has been much discussed,

[1] A shallow conical cup, 4 to 5 cm. in diameter, joined with a short stem, is suggested. An ordinary glass funnel of these dimensions may, however, be used.

and is still open for debate. It should be recalled that whenever the fluid in any branching system is set in motion reflected waves are sent back from the periphery. That such reflections are probably present in the arterial system can, *a fortiori*, be inferred from the fact that the presence of the blood corpuscles favors such a reflection. Without entering into the contradictory evidence of the past, it may be said that it has been firmly established that reflected waves cannot primarily be responsible for the dicrotic notch and wave, for in optical records of the aortic pressure the incisura goes hand in hand with valve closure, and when reflected waves appear at all they occur much later in diastole. It would seem, therefore, that the dicrotic notch and wave are the representatives of the incisura and after-vibration in the peripheral pulse.

Frank, however, finds difficulty in interpreting the dicrotic wave as merely the incisura and after-vibration modified in transmission, for the dicrotic wave becomes larger toward the periphery and all other waves submitted to the same frictional influence become smaller. He, therefore, believes that its amplitude is augmented by a resonance effect with other vibrations reflected from the periphery.

Out of this discussion grow two very important practical facts: (1) We must distinguish between the *central pulse*, as it is recorded from the subclavian or the lower carotid arteries, and the *peripheral pulse* as it is recorded from the radial artery; (2) on account of the poor transmitting ability of the arterial system, the *peripheral pulse reproduces only inaccurately the pressure changes established in the aorta, and consequently it may be anticipated that its diagnostic value will be correspondingly less.*

CLINICAL SIGNIFICANCE OF CENTRAL ARTERIAL PULSE TRACINGS.

Since a comprehensive clinical study as to the value of the central arterial pulse remains to be undertaken, the probable information that may be obtained by such studies must for the present rest largely upon results obtained from experimental animals where known circulatory variations are induced (v. Born, Biaudet and Weckman, C. Tigerstedt, Wiggers and associates), and, to a limited extent only, upon pulse tracings obtained from patients. The information yielded depends: (*a*) On changes in contour and (*b*) altered time-relations.

Accidental Contour Changes.—Before attaching significance to contour changes, it is necessary to recognize deformations due to extraneous causes and, as far as possible, develop technic which avoids them. As the author has had occasion to superintend the taking of central pulse tracings by students during the last nine years, during which time excellent, medium and poor records from 480 different students have naturally come under observation, he believes it possible to state

the most common causes of unreliability and suggest means for their avoidance.

Distortions of subclavian records are essentially due to: (*a*) Superposition of venous waves; (*b*) abnormalities resulting from respiratory movements; (*c*) the exertion of insufficient pressure over the subclavian artery, and, less frequently, (*d*) muscular contractions or irregular pressure.

Owing to the fact that the venous pulse is more prominent in the recumbent position, it is almost if not quite impossible to obtain uncomplicated tracings of the subclavian pulse in many individuals in the lying posture. It is absolutely impossible, when venous pulse waves are abnormally accentuated, in pathological conditions of the heart. The sitting position is, therefore, to be preferred, although it is permissible to employ a semireclining position in bed or in a Morris chair. When present such venous waves are, however, readily recognized and do not necessarily render the records worthless—a fact which is fortunate in many clinical conditions where pure records cannot be obtained. Such curves are distorted by a large presystolic and a large diastolic wave (Fig. 70, *II*). If firm pressure is employed the contour of the systolic ejection phase is unaffected and time relations may be easily calculated.

Ordinary respiratory movements usually only affect the curves by causing them to move up or downward. Occasionally, however, they distort the contour of the curves, which can readily be recognized by the fact that consecutive waves have varying contours. It is, therefore, preferable to record curves during voluntary apnea, which need be maintained only five or six seconds in order to record a short series of waves. When dyspnea is present the curves are worthless. As patients with cardiac disease often find it impossible to hold the breath without other muscular movements creeping in, records cannot be obtained from an occasional "cardiac" patient.

One of the chief causes of unsatisfactory records is due to the fact that insufficient pressure is exerted. This is the error most frequently made by the novice. The curves (Fig. 70, *III*, *IV*) then show either: (1) A sharp triangular impact during ejection and a smaller dip at the beginning of diastole or (2) a more or less typical venous pulse from the subclavian vein. The latter happens when the patient is reclining or when the venous pulse is unusually prominent—even in sitting positions. Such records cannot be used for studying contour changes. In order *to obtain good records the receiving tambour must be in absolute apposition with the skin, so that no leaks occur, and must be applied with considerable pressure behind the clavicle;* indeed, the pressure must usually be somewhat uncomfortable in order to be adequate. The more vigorous the venous pulsations the greater the pressure necessary to eliminate them.

Finally, distortion due to muscular contraction of the subject and

irregular pressure of the operator's hand must, of course, be eliminated. The subject should sit perfectly relaxed, with chin down and eyes directed straight forward. The natural tendency of the patient to be helpful by raising the chin, tilting the head backward and rotating it to the opposite side must be discouraged, as this serves not only to render all the neck muscles tense, but also introduces irregular jerks. Fortunately, these are readily recognized on tracings.

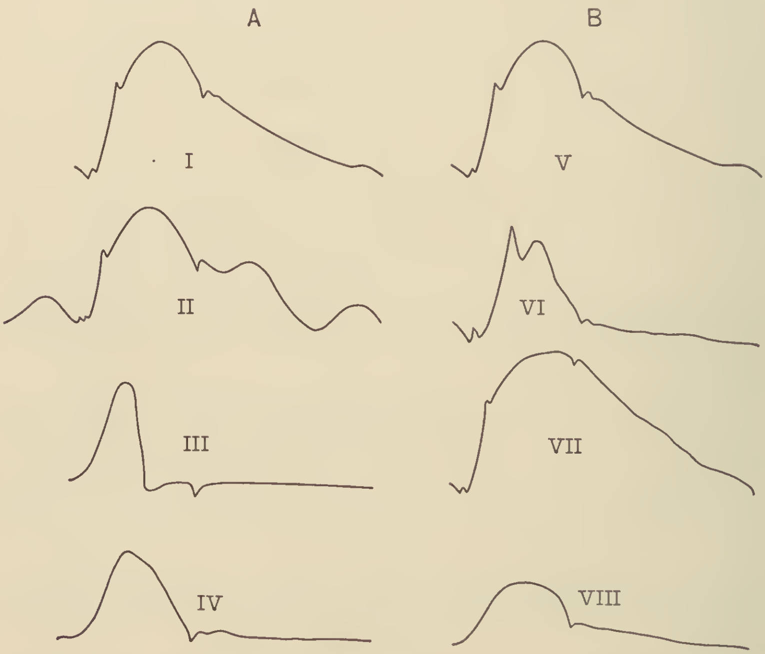

FIG. 70.—*A*, series of supraclavicular arterial pulse waves, showing how recorded pulse waves may be deformed, owing to improper technic. *I*, normal; *II*, appearance when venous elements are added; *III*, appearance when gross leakage exists in system; *IV*, impact curve resulting when slight leakage or too light pressure applied over artery. *B*, series of waves, showing inherent changes in contour with different circulatory conditions. *V*, normal; *VI*, low resistance pulse; *VII*, high resistance pulse; *VIII*, small systolic discharge pulse.

Inherent Variations in Contour.—While the detailed vibrations and pressure changes may be retained under a variety of conditions, they may be intensified or diminished under certain circulatory conditions. The degree to which the vessels are stretched—in other words, the height of the diastolic pressure—affects the amplitude of the primary oscillations (Fig. 69, *d*–*e*). Under states of decreased diastolic distention the blood column on ejection is thrown with greater vigor, and consequently the oscillation is magnified (Wiggers, C. Tigerstedt).

When the vessels are distended this notch may be much reduced and, in fact, may be indicated only as a halt on the ascending limb.

The contour of the systolic trapezoid depends on the relative volumes of cardiac ejection and peripheral outflow. In the normal pulse the curve continues to mount as long as the systolic ejection volume exceeds the arterial inflow; when the latter is greater than the former the curve begins to decline. Consequently, under conditions of altered peripheral resistance the contour changes.

In accord with these principles, one may recognize several types of pulse curves as showing characteristic deviations from normal. They are shown schematically in Fig. 70, *B*.

1. *Low-resistance curves,* in which the primary oscillation is large, prominent and has a longer period, and in which the rest of the curve rises to a second sharp peak and then progressively declines, giving a triangular appearance to the curve. The incisura occurs low on the curve, and in some cases it is difficult to distinguish its onset clearly. (Fig. 70, *VI*.)

2. *High-resistance curves,* in which the primary vibration is small, of short duration or indicated as a mere jog, and in which the pressure rises more gradually to a summit almost throughout systolic ejection, declining slightly toward its end. A broad trapezoidal shape is suggested. The incisura is sharp and followed by small, sharp aftervibrations. (Fig. 70, *VII*.)

3. *Reduced-output curves,* in which the curves become more rounded and lose their characteristic sharp vibrations. The curve rises slowly to a rounded summit and equally slow declines. (Fig. 70, *VIII*.)

In addition to these types of pulse recorded when no organic lesions of the heart or large vessels obtain, characteristic pulse contours may be recorded when such lesions exist. Their detailed characteristics, as far as they have been established, will be discussed in the appropriate chapters of the last section.

Low-resistance pulses have been recorded by the author and others in the following types of clinical cases without organic heart lesions, viz., after amyl nitrite administration, in typhoid fever, exophthalmic goiter and hemorrhage. Similar curves have also been obtained in cases of aortic aneurysm and aortic insufficiency.

High-resistance pulses are common in conditions of hypertension accompanying nephritis or arteriosclerosis (Fig. 75, as my records show, was taken from a patient with a systolic pressure of 185 mm.). The curves of aortic stenosis resemble these records in certain respects only (*cf.* page 549). Reduced output pulses are common as terminal events and during decompensating mitral lesions. This list will, no doubt, be added to, as the method is more extensively employed clinically.

Significance of Time Relations.—From the central arterial pulse (but not from the peripheral radial pulse) we are able to calculate:

(1) The duration of systole (*a–g*, Fig. 69); (2) the duration of diastole (*g–a*); (3) frequently the isometric contraction phase (*a–b*); (4) the ejection phase (*b–f–g*); (5) the isometric relaxation phase (*g–h*).

Of these the duration of the ejection phase is most readily determined and is of the greatest importance. Experimental work (Wiggers, Wiggers and Katz) has shown that when the duration of systole alters, the isometric phase is affected relatively little, but the systolic ejection phase is predominantly concerned.

In discussing the clinical importance of variations in the phase of systolic ejection it is important to recognize that the *absolute duration* of this phase cannot be considered, owing to the fact that it varies in normal individuals with the length of previous diastole. Consequently, we must have some means of knowing what the anticipated duration of these phases is at different cycle lengths or, what amounts to the same thing, at *different* heart rates.

The relation of systole to diastole or cycle length (the so-called *s/c* ratio) or to heart rate has been frequently investigated in man, and has been expressed by general statements, by curves or by formulæ (*cf.* page 103). The writer has not had the opportunity to test the validity of all these formulæ, but is ready to indorse the formula of Lombard and Cope, which, for the sitting position, reads $S = \frac{60}{26\sqrt{R}}$, in which R represents the heart rate. The reliability of such a formula may be tested by plotting a curve by its use, as shown in Fig. 71, and relating to it the actual systoles found in different normal subjects. Doing this, Lombard and Cope found that in 620 tests made on 250 men, the actual systoles in 94 per cent of cases deviated from this formula not more than 0.02 second and the remaining 6 per cent not more than 0.025 second. It should be remembered, however, as Lombard and Cope themselves have pointed out later, that their method measures not the entire systole but approximately the duration of systolic discharge, which, as a matter of fact, is fortunate, since it is with this phase that we are particularly interested. To further test the applicability of this formula the writer and his laboratory associates have similarly plotted, in relation to such a plotted curve, the actual durations of the ejection phases at different rates calculated from optically recorded subclavian pulses. A total of 450 records from as many normal men have thus been related, with the result that in only 7 per cent of cases do the figures deviate more than 0.02 second from the curve established as in Fig. 71. Our results indicate, however, that this holds only between heart rates of 55 and 95 per minute, the relative duration of systolic ejection being definitely less, at more rapid rates.

It is, therefore, possible to establish the duration of systolic ejection in clinical cases and, by relating these either to the duration of the entire cycle or heart rate (if regular), to determine how they compare

with rates found in large numbers of normal individuals. We can then say that *when the duration of systolic ejection is more than* 0.02 *second to either side of the duration, established by such a curve, abnormal relations probably exist.*

Searching experimental inquiry (Wiggers and associates) has indicated that a permanent, persistent lengthening of systolic ejection occurs only when the initial pressure or diastolic distention of the heart is increased. This may occur as a result of an increased venous return, or when the ventricles are required to contract against an arterial resistance so great that a retention of blood and consequent dilatation occurs.

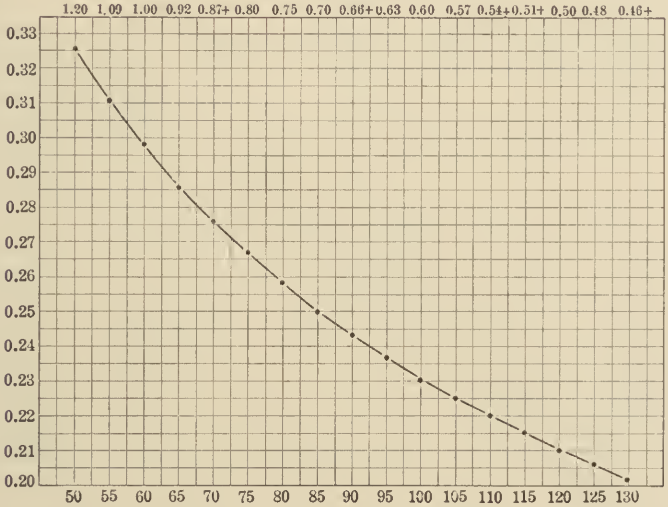

FIG. 71.—Curve plotted on basis of Lombard and Cope's formula, showing at a glance the theoretical durations of systole at any heart rate or cycle length. Ordinates, duration of systole; abscissæ, *below*, in terms of heart rate; *above*, in terms of cardiac cycle length.

Consequently, the probable suggestion may be made that an increased duration of systolic ejection indicates that the ventricle is required to work harder and that it does so by virtue of a greater diastolic distention. When arterial resistance, as indicated by diastolic blood-pressure, is not unusually high, such a lengthening further indicates that the heart is discharging larger volumes. (For detailed physiology, *cf.* page 109.) This criterion is especially valuable, as it will be noticed, in considerations entered into above, we have no typical contour curves which alone are characteristic of increased systolic discharge.

A decreased phase of systolic ejection, on the other hand, may not with equal certainty be held to indicate a reduction of systolic dis-

charge. This is so largely because without changes in venous pressure an increased activity of the accelerator mechanism as well as changes in the blood gases tend to abbreviate systole more than it should according to theoretical laws. Furthermore, the possibility that variation in the epinephrin control may similarly act to abbreviate systole cannot be considered as entirely eliminated.

Investigations as to the clinical applicability of these deductions from experimental work have just begun. Katz and Feil, in studies just completed but as yet unpublished, found that at comparable cycle lengths, systole is definitely shorter than normal in cases of auricular fibrillation. Whether this is due to an impaired ejection resulting from primary myocardial derangement or to the absence of auricular systoles has not so far been determinable.

Variations in the Isometric Contraction Phase.—While certain initial vibrations are usually recognizable in the arterial pulse curves during the isometric phase (*e. g.*, Fig. 69, *a–b*), more extensive experience has shown that the beginning of this phase is not always accurately indicated by the first vibration (*cf.* C. Tigerstedt, Wiggers). As these vibrations sometimes begin with a negative wave and again with a positive deflection, one is often puzzled to know what vibration to consider as the first occurrence during the isometric phase. For these reasons it is desirable to record synchronously some evidence of primary ventricular activity. The usual proceeding has been to record synchronous apex and carotid tracings and, after allowing approximately for the transmission time of the arterial pulse, to calculate the time difference (Edgren). The inherent inaccuracy in this method consists, of course, in the fact that the delay in the arterial pulse cannot be definitely determined. Furthermore, it is sometimes difficult to recognize the onset of ventricular systole in the apex curves.[1] When, in addition, these records are recorded on smoked surfaces, lag in lever movements must render such results still more inexact. The writer has, therefore, suggested central pulse curves as more exact, and in association with Clough has suggested a method by means of which the transmission time of the pulse may be directly corrected on such tracings:

The main vibrations of the first sound coincide with the beginning of the ventricular pressure rise and, therefore, mark the onset of the isometric period. The vibrations of the second sound fall a short interval after the end of systole and correspond with the bottom of the incisura of the pressure curve in the aorta. To correct accurately for delay in transmission of vibrations to the neck, it is necessary, therefore, to place a pair of dividers with one point on the onset of the first sound vibrations and the other on the second-sound vibrations and transfer the set dividers to the carotid curve so that one point is

[1] Recently this difficulty has again been emphasized by Bazett and Dreyer and means for overcoming it suggested.

placed at the bottom of the incisura. The other point then cuts the wave representing the beginning of the isometric period. The interval between this mark and the rise of the primary wave gives the isometric period, while the distance from this mark to the beginning of the incisura gives the duration of the total systole. It is obvious that the correct interval for systole so determined is slightly shorter than the interval between the onset of the two heart sounds.

Results of Various Observers and Their Methods.

By Cardiogram and Carotid Pulse Corrected for Transmission.		
Rive	1866	0.073
Landois	1872	0.085
Keyt	1887	0.06
Edgren	1889	0.087–0.093
Hürthle	1891	0.06
Schmidt	1893	0.020–0.040
Jaquet and Metzner	1901	0.020–0.030
Robinson and Draper	1910	0.070–0.085
By Differences between Heart Tone at Apex and Base.		
Einthoven and Geluk	1894	0.06
By Preliminary Oscillations of Central Pulse.		
Tigerstedt	1908	0.051
Wiggers	1914	0.058–0.085
By Simultaneous Heart Sounds and Subclavian Pulse Tracings.		
Wiggers and Clough	1919	0.025–0.080 extreme range 0.040–0.060 average range
Katz and Feil	1923	0.024–.089 extreme range 0.035–.070 average range

Clinical Significance.—It is apparent that while figures for the normal isometric contraction phase vary considerably, it is probable that figures outside of the ranges 0.04 to 0.06 second must be referred either to technical inaccuracy or be held to indicate abnormal lengths.

Experimental work has shown that this phase of cardiac contraction is relatively constant. *A priori* considerations would lead one to infer that the height of pressure in the aorta at the beginning of ejection might modify this phase. Thus, we may suppose that the higher the arterial pressure at the beginning of ejection the longer the contraction interval required to open the semilunar valves. Experimental work indicates, however, that while occasionally an increased arterial resistance does lengthen this interval by 0.01 or 0.02 second, the change is often absent or the interval may even slightly decrease (C. Tigerstedt, Weitz and Graner, Wiggers). If, however, the resistance is more centrally applied, as in compression of the arch of the aorta or

in aortic stenosis, the interval is distinctly increased. The interval has likewise been supposed to increase greatly when a mitral regurgitation exists, but the experimental work of Feil and the author indicates that this is not the case. Hürthle first pointed out that probably the duration of the phase is much more dependent on the initial intraventricular tension, an elevation of tension decreasing this period. While this interpretation is borne out by observations of the writer, the magnitude of the change in some experiments is very trifling. Changes in rate likewise have no great influence.

In general, it is doubtful if changes in the isometric contraction phase greater than 0.02 second can occur as a result of altered dynamics alone. There are only two experimental conditions during which pronounced lengthening of this phase takes place, viz., in a hypodynamic or failing heart and in experimental aortic stenosis. On this basis, an undoubted lengthening of the isometric phase in clinical cases may be considered as indicating an impaired myocardium or the existence of some excessive obstruction to the ejection of blood or both (*cf.* Robinson and Draper, Geigel, Pezzi, Weitz).

CLINICAL SIGNIFICANCE OF RADIAL PULSE TRACINGS.

We may now analyze the ways in which the radial pulse curves are of value in determining the condition of the heart and circulation and how their study may, in turn, aid in the art of palpation. For practical purposes we may discuss: (1) Changes dealing with time relations of the pulse and (2) those dealing with its conformation.

Temporal Relations of the Pulse.—Rate.—One of the important points to be determined about the pulse is its rate. In doing this the graphic record has only the advantage that very small pulses which are not palpable may be recorded. This is due to the fact that the sensation transmitted to the finger is determined largely by the suddenness of the impact, consequently the smaller waves, which are much more rounded and gradual in their rise, make no impression on the tactile sense.

The pulse rate usually corresponds to the heart rate. Frequently, however, a deficit in the pulse beats exists. This occurs when the ventricles give contractions too feeble to open the semilunar valves or when the pulse wave is so weak that it does not reach the wrist (*cf.* Fig. 165). Such a *pulse deficit*, as the condition is termed, may be suspected when the pulse beats are irregular in size or uneven in rhythm and when the pulse count is low. The exact deficit may usually be determined by comparison with the apex beats, when palpable, or listening to the heart sounds. Only a single sound occurs in cases of weak systoles unaccompanied by the opening of the semilunar valves, whereas two sounds are audible when the pulse deficit is due to an impaired transmission. A source of error readily occurs in interpreting

the first sound of a feeble contraction occurring early in the diastole of the preceding beat as a reduplicated sound.

Since the pulse rate, with these exceptions, corresponds to the rate of cardiac contraction it can give information as to the latter. To recognize clearly the nature of the information given, it is necessary to bear in mind that the bulk of evidence indicates that the beat of the heart originates within the *S–A* node, is transmitted thence by the His-Tawara system to the ventricles and causes their excitation. The rapidity with which impulses are initiated, however, and the speed with which they are conducted are modified by the central nervous system through two types of antagonistic fibers, the inhibitory and the accelerator fibers. The former pass in the vagus trunk and tend to slow the rate, the latter run in the sympathetic chain and exert an accelerating influence (*cf.* page 48).

It is apparent that the heart rate may be modified as follows:

(*a*) Through stimulation or inhibition of the vagus system.

(*b*) Through stimulation or inhibition of the accelerator system.

(*c*) Through inherent change in the rhythm production or impulse propagation in the heart itself.

Causes of Rate Variations.—In most text-books of diagnosis and physiology are to be found tabulations, more or less complete, of conditions and diseases which are accompanied by abnormal pulse rates. These need not be reconsidered here.[1] The reasons for many of these disturbances are not as yet proven experimentally but rest largely on a theoretical basis. In a few cases, experimental relations between pulse rate and other facts have been determined and the table appended represents some of these in classified form. Slowing of the heart may be due to:

A. Stimulation of the vagus center.
  1. Directly by:
    (*a*) Mechanical means: as
      Rise of intracranial pressure.
      Intracranial tumor pressure.
      Increased blood supply.
    (*b*) Toxic substances: as
      Bile.
      Lead, digitalis, adrenalin.
      Products of asphyxia.
  2. Indirectly by:
    (*a*) Influences from higher cerebral areas (epilepsy, hysteria).
    (*b*) Reflexes from the digestive tract (*via* vagus).
    (*c*) Reflexes from the bloodvessels and heart.

[1] For detailed analysis of factors causing heart-rate changes, see Hering: Pathologische Physiologie, 1921, p. 8. Tigerstedt: Physiologie des Kreislaufes, 1921, **2**, 429.

B. Stimulation of the vagus nerve.
Pressure in neck, vagus tumors, vagus neuritis.
C. Alteration in cardiac muscle.
Toxic myocarditis (diphtheria, etc.).
Heart-block, nodal rhythm, etc.
D. Paralysis of the sympathetic (rare).
Thoracic cord lesions, pressure.

Acceleration of the heart occurs as a result of:

A. Stimulation of the sympathetic system, or depression of the cardio-inhibitory center, resulting from:
(*a*) Decreased blood supply:
Anemia.
Hemorrhage.
Splanchnic dilatation.
Intestinal disturbances, baths.
(*b*) Drugs, toxins.
(*c*) Reflexes:
Exercise, general vasodilatation, hemorrhage.
(*d*) Cerebral influence:
Emotion.
Fright.

B. Depression or paralysis of the peripheral mechanism, *e. g.*, atropine.

C. Stimulation of the heart itself.
(*a*) Mechanical means (failing compensation).
(*b*) Thermal means (fevers).
(*c*) Toxic products (infections, drugs).
(*d*) Functional disturbances (tachycardia).

Pulse Rhythm.—If the time intervals occupied by consecutive cycles are approximately equal, as in the normal pulse where they vary only slightly with the phases of respiration, we speak of a *rhythmic pulse.* If they are not equal, however, the pulse is said to be *arrhythmic.* Although other and simpler aids now exist for clearly determining the causes of irregular heart action, it is frequently possible, when a single disturbance exists, to obtain evidence of the nature of the irregularity by a careful study of the radial pulse curves alone (Wenckebach).

Arrhythmias of the heart have been divided on the basis of arterial pulse curves into: (*a*) The allorhythmias and (*b*) the complete arrhythmias. In the former there is a distinct order or periodicity in the recurrence of certain wave groups, while in the latter no such order exists.

The following are some of the most common and typical forms of irregularities which are illustrated in the curves with corresponding letter in Fig. 79. The nature and causes of these irregularities as well as others of rarer and more complicated character are discussed in a later chapter.

I. **Regular Arrhythmias (Allorhythmias).**—A. *Sinus arrhythmia,* due to a variation and alternate influence of vagal inhibition and excitation of the "pacemaker." They are characterized by a progressive increase and decrease in the length of the cardiac cycle. Occasionally the long pauses are so lengthened that we may speak of a temporary cardiac standstill. When the variations occur so that acceleration falls approximately during inspiration and retardation mainly during expiration, it is spoken of as *respiratory irregularity.* When the variations occur regularly, or irregularly without regard to the respiratory activity, it may be designated as *phasic sinus arrhythmia.*

B. *Premature ventricular contractions or extrasystoles*—due to an excessive irritability of the ventricle or the presence of abnormal stimuli. They are characterized by the presence of a premature small wave, x, or the absence of a wave, x'. In either case the extracontraction is followed by a compensatory period of such length that the normal and premature waves approximately equal in length two normal waves, $2\ T$. Such a pulse group is termed a *full bigeminus.* Each smaller wave and compensatory pause is followed by a large arterial beat, p.

C. *Premature auricular systole*—due to the origin of a premature impulse in the auricle which, when transmitted to the ventricles, gives a premature ventricular contraction as well. The premature ventricular contraction is characterized by a small wave, x, or, when it occurs very early, by a pause, as shown in curve D at x. The auricular origin of the extrastimulus is evidenced by the fact that the interval following is not so long that with the preceding beat it equals two pulse cycles, *i. e.,* $T < T'$. Such a group has been termed a *shortened bigeminus.*

D. *Paroxysmal tachycardia*—a sudden acceleration of the heart preceded by a few extrasystoles of auricular origin (*e. g.,* at x, $T_2 > Tx$).

E. *Incomplete sino-ventricular block* (usually called A–V block).—This condition can be most definitely determined from the arterial pulse when the ventricle regularly fails to respond to a sinus stimulus. The rhythm is then regular but slow. When the block is irregular (*e. g.,* 2:1, 3:1) it is usually found that some short pulse wave is continued in the longer waves a definite number of times. Thus, m is contained twice in n and three times in o.

F. *Complete heart-block*—due to the complete blocking of impulses from the sinus region and the establishment of an independent ventricular rhythm. The pulse is slow and rhythmic. Careful measurements show, however, that the intervals vary somewhat.

II. **Irregular Arrhythmias.**—G. *Auricular Flutter.* A condition in which the auricle contracts at a very rapid rate, but the ventricle responds irregularly. The arterial pulse in this condition is on the border between an allorhythmia and complete arrhythmia. On superficial inspection the registered arterial pulse appears quite rapid and completely irregular both in rhythm and sequence of beats. In some

instances a scheme of regularity may, however, be made out, for the long wave lengths are often multiples of the shortest waves; but the correspondence in these cases is not very exact, so that it seems preferable to class this with the completely irregular pulses.

II. *Auricular fibrillation*—a fibrillation of the auricles, in which the ventricles beat in a rapid but absolutely irregular manner. The pulse is irregular in size and rhythm and the amplitude of beats bears no relation to the previous diastoles, as is the case in extrasystoles.

Variations in Conformation.—The changes in the conformation of the radial pulse consist in alterations in size and outline.

Amplitude.—The amplitude of the pulse waves is determined in a considerable measure by adjustment of the apparatus which, even though it may record faithfully the variations in pressure, does so without abscissæ. Nevertheless, it is found by practice that when the best possible adjustment is made each instrument records a tracing which is quite constant in amplitude in normal individuals. For three different instruments used upon students the following averages were obtained:

Jaquet, old pattern.	Jaquet, new model.	Dudgeon.
9 mm.	7.3 mm.	13.3 mm.
48 cases	23 cases	23 cases

A large oscillation may be due either to a large output, a slow rate, a low peripheral resistance, a poor filling of the arteries, as in hemorrhage, or a low degree of arterial tonus. A small oscillation occurs when the output is small, the rate rapid, the resistance high, the arterial tonus great or the elasticity impaired by arteriosclerotic changes (*cf.* Fig. 203).

When the size of the consecutive pulse beats varies we speak of an *unequal pulse*. The normal pulse waves are not exactly equal. This is due, in part, to the fact that the mechanical effect of respiration modifies the ventricular output. When the pulse is regular the amplitude usually decreases during inspiration and increases during expiration. When, however, the rhythm varies during the respiratory phases, so that the cycles become shorter in inspiration and longer in expiration, the amplitude decreases in inspiration and increases in expiration (see page 128). Variations in size may occur, however, in perfectly regular pulses, as is the case when the filling of the heart or the output is periodically obstructed—for example, in pericardial adhesions, effusions and tumors, etc. In such cases the pulse may become exceedingly small or be entirely absent during inspiration, giving rise to the so-called *paradoxical pulse* (*cf.* page 627). Lastly, it may occur when the vigor of cardiac contraction is inherently modified, as in *pulsus alternans*. In this condition every alternate beat is smaller, and when any difference in spacing occurs, the smaller beat has the shorter cycle (*cf.* also page 505).

Irregularities in size are also associated with irregularities in rhythm. As a rule, the longer a certain cycle the larger the pulsation following, and *vice versa*. This is due, in part, to the fact that the output of the heart depends upon the interval of diastolic filling, but also to the fact that the diastolic pressure is allowed to fall more during the longer interval.

Form of Pulse.—In forming an estimate of the clinical value of the pulse form it must be remembered that the instruments in common use are utterly incapable of recording the pressure variations present in the arteries. Any deductions drawn from such studies are entirely fallacious. It is, therefore, not to be wondered at that different clinicians have reached very different conclusions as to the diagnostic value of the pulse shape. The records taken with optically recording sphygmographs are as yet exceedingly few in number. We shall confine ourselves, however, entirely to the variations in form of the peripheral pulses so obtained (Hewlett, Feil and Stroud). In the study of variations in form we are concerned with the rise, the fall and the position and size of the dicrotic wave.

Variations in the Rise.—It can readily be shown by an adjustable artificial circulation scheme that the gradient of the rise is determined: (*a*) By the rate of discharge; (*b*) the volume of discharge per beat, and (*c*) by the size of the aortic opening (Fig. 174). Furthermore, it is dependent on the height of the diastolic pressure. It is also possible to show this in experimental animals, and more especially to prove that in conditions such as aortic stenosis the wave rises slowly and is rounded or flat-topped. Similar pulses have been recorded in man. The rise is steep after administration of nitrites and in fevers (Hewlett). It is especially rapid when the pulse is very slow, *e. g.*, in heart-block. In aortic stenosis the rise is very gradual, as shown in Fig. 181.

In 1912, Friberger and Veiel reported curves, both from the central and from the radial pulse, in which the steepness of rise was less and in which a rounded top and ascending systolic plateau replaced the descending plateau found in normal pulses. The better transmission of the central changes to the peripheral vessels in arteriosclerotic cases may be explained, perhaps, by the fact that the arteries more nearly resemble solid tubes.

Anacrotism.—Occasionally it is found that instead of a smooth ascending limb, a break or jog occurs on the ascent which is designated as the *anacrotic notch*. It has been observed in cases in which the artery is partially compressed centrally (for example, by a tumor), in cases of aortic stenosis, arteriosclerosis, aortic aneurysm and occasionally in aortic insufficiency.[1] Various explanations have been forthcoming. It has been regarded as due to an "irregular" or "jerky" contraction of the ventricle (Nicolai), to a high arterial pressure (Sahli),

[1] *Cf.* Figs. 181 and 185.

to the nature of the arteriosclerotic vessels (Lüthje), to a rapid reflection of peripheral waves, etc. A general theory to explain its occurrence in different conditions has been offered by Schönewald, recently: Whenever the volume-elasticity of the aorta or large arteries is so changed (for example, in aneurysm, compression, arteriosclerosis or high pressure) that further expansion is not possible at the onset of systole, the ejected blood is moved onward to the periphery, causing the rise of the radial curve. As the pressure continues to rise, the aorta finally dilates toward the end of systole and the pressure is distributed less slowly to the periphery, causing the notch and slower rise. It is possible, however, as Lewis has shown, to produce anacrotism by peripheral factors alone, so that its diagnostic value remains in doubt.

Variations in Descending Limb.—The descending limb of the pulse wave may vary greatly in its slope. The significance of this is greater than of the variation in the rise. It is readily shown by pulse tracings, taken on an artificial circulation model, that the gradient of the pressure fall becomes steeper when the peripheral resistance is lower, when the arterial wall is thicker and when an insufficiency of the aortic valves is created (Fig. 174). Similarly, it can be shown experimentally (v. Born, Biaudet and Weckman) that when the peripheral resistance is decreased by depressor influence or nitrites the slope of the descending limb of the carotid becomes more rapid, while it becomes more gradual after the intra-arterial injection of adrenalin or after clamping of the abdominal aorta. Also, it can be shown that the descending limb drops more rapidly after the induction of aortic insufficiency in experimental animals (Fig. 183). Similar curves have been recorded in man (Figs. 112 and 185).

There seems to be no question that a rapid slope of the descending limb of the radial is often associated with a low diastolic pressure and, when present, no doubt often indicates such a pressure. More accurately stated, however, the rapid decline signifies that diastolic pressure is relatively low as compared with the systolic pressure. Thus, it may occur when the diastolic pressure remains unaltered, but the systolic pressure is high, as happens when rigid arteries are insufficiently distended during systole or when the systolic output from a hypertrophied heart is great and rapid so as to produce a higher systolic pressure and a more rapid peripheral flow. The low diastolic pressure explains the rapid drop found in aortic insufficiency, which is so marked that it can generally be appreciated by palpation (Figs. 112 and 185). It may be added, however, that some cases of aortic insufficiency in which the pulse gives a distinct collapsing impression to the finger are found, on investigation by optical sphygmographs, not to possess such a fall, the palpating finger being evidently misled by the sudden impact (Fig. 112) (*cf.* also Feil and Stroud).

Variations in Dicrotism.—The significance of the depth and prominence of the dicrotic notch and wave has given rise to extensive

discussion. Before attempting an analysis of dicrotism it is necessary to realize that a pulse may appear dicrotic when it is not really so from a physical viewpoint (Lewis). Thus, if we place dicrotic notches of the same magnitude on three pulse skeletons, as shown in Fig. 72, no *real dicrotism* occurs (that is, ab, $a'\ b'$, $a''\ b''$, etc., are equal), but the middle curve apparently displays an increased dicrotism. It is obvious that this form of *apparent dicrotism*, to which clinicians obviously refer, is determined by the relative position of the dicrotic notch on the descending limb—being increased whenever the descending limb falls more rapidly and diminished when it falls slowly.

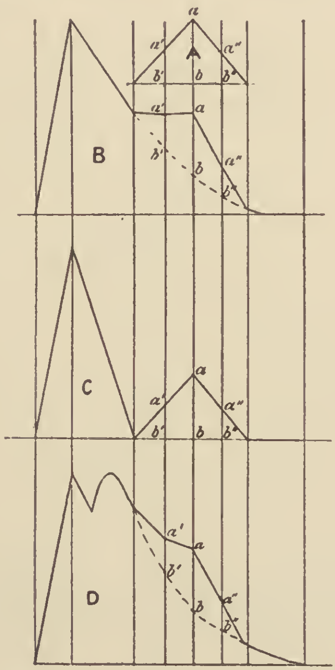

FIG. 72.—Schematic figure illustrating "apparent dicrotism" when real dicrotism does not exist. Dicrotic wave, A, superimposed upon the descending limbs of three primary waves, B, C, D, so that ab, $a'\ b'$, $a''\ b''$, etc., are equal. (After Lewis.)

Since a rapid fall, as before pointed out, occurs frequently when the diastolic pressure is low in consequence of low peripheral resistance, a large dicrotic is usually found in such conditions (amyl nitrite and typhoid pulse). The dicrotism may be real instead of apparent. This is due, in part, to the fact that the arterial walls oscillate at a larger amplitude at lower pressures and in part to the fact that the interference or resonance with peripherally reflected waves is altered (*cf.* Figs. 141, 142 and 201).

Increased dicrotism, like the rapid diastolic collapse, is not neces-

sarily associated with low diastolic pressure or relaxed arteries as is evident from its occurrence in conditions of high systolic pressure (for example, arteriosclerosis and nephritic hypertension). It occurs here in association with a rapid fall because the rigid arteries are imperfectly distended by the rapid systolic output from a hypertrophied ventricle and, in consequence, a systolic pressure relatively high, as compared to diastolic, is created. From this analysis it seems that increased dicrotism should be the invariable accompaniment of a more rapid fall of the pulse wave. Such, however, is not exactly the case, for it must be remembered that its position and amplitude are governed not entirely by the depth of the incisura in the central pulse, but partially, also, by resonating reflections. Any influence tending to increase this resonating effect likewise increases the amplitude of the dicrotic wave, and, *vice versa,* any diminishing agent acts accordingly upon the amplitude. Finally, it should be remembered, in interpreting dicrotism in the clinic, that *many of the ordinary forms of sphygmographs employed actually record no dicrotic notch, but instead show mere after-vibrations of the lever in the descending limb.* When it happens, for example, that after amyl nitrite the pulse accelerates, the requirements of the instrument are increased and the lever is thrown into greater oscillations, so that the *so-called dicrotic notch* markedly increases in amplitude, owing to greater lever throw. This, in a large measure, explains why the pulse records taken by various observers during fevers and aortic insufficiency, when the pulse is large, are sometimes accompanied by great and sometimes by little dicrotism, and why the significance of dicrotism has received such varied interpretation.

Transmission Time and Velocity of the Pulse Wave.—The transmission time of the pulse is estimated by the difference in time between two pulses, such as the radial and brachial or the radial and the subclavian (Fig. 69). By obtaining the distance as accurately as possible the velocity may be computed. The velocity of the pulse has been used as a functional test for determining the elasticity of the artery. This is based on the formula of Moens that the propagation $M = K\sqrt{g\frac{E\,a}{\triangle\,d}}$, in which K is a constant, g = the acceleration due to gravity, E = the elasticity coefficient, a = the thickness of the arterial wall, d = its diameter and $\triangle$ = the density of the fluid. In this formula the variations in the specific gravity may be neglected. Thus, if the specific gravity of the blood at 1.005 yields a pulse velocity of 10 meters per second the time of transmission at 1.035 specific gravity would be 10.09 meters per second. Recently, Bramwell and Hill have modified the Moens formula to read:

$$v = 3.57\sqrt{\frac{V}{dv/dp}}$$, or stated in a simpler form:

$$\text{Velocity} = \frac{3.57}{\sqrt{\text{Percentage increase in vol. per mm. increase in pressure.}}}$$

So stated, the velocity of the pulse becomes an inverse function of the extensibility. The extensibility of the vessels is not only a function of the character of the wall, however, but depends to a very considerable extent on the diastolic pressure as well as the caliber of the arteries examined. Thus, Bramwell and Hill have recently shown on isolated carotid arteries that the pulse velocity ranges from 3.76 meters per second at diastolic pressures of 25 mm. Hg. to 18.5 meters per second when the diastolic pressure was 200 mm. Hg. Similarly, other investigations have shown that in man the pulse velocity changes when the arterial pressures are modified by drugs (Bazett and Dreyer). Nevertheless, it appears probable that when standard comparisons are made, as between radial and carotid pulses, and when, furthermore, cases with comparable blood-pressures are compared, the pulse velocity is capable of supplying valuable information as to the character of the arterial walls.

Figures of pulse velocity obtained from radial and carotid tracings of normal adults are gathered together in the following table:

Year.	Investigator.[1]	Meters per second.
1864	Czermak	6.70
1878	Moens	8.70
1879	Grunmach	8.29
1887	Keyt	7.37
1889	Edgren	7.63–7.32
1889	Horweg	9.00
1912	Münzer	9.00–12.0
1912	Friberger	6.70– 9.4 (men) 7.00–10.0 (women)
1912	Ruschke	9.00
1921	Laubry, Mouget and Giroux	8.00
1922	Bramwell and Hill	6.00–7.40
1922	Bazett and Dreyer	7.00

These results indicate that, while it may be said in a rough way that the arterial pulse travels from the innominate to the radial artery with an average velocity of 7 to 8 meters per second, variations as great as 2 meters per second occur in the results of different observers. This is, of course, partly a matter of technic, though the variable diastolic pressures and inherent changes in tonus in different individuals, no doubt, plays a great rôle (Dawson; Laubry, Mougeot and Giroux). The velocity is lowest in the young and increases gradually with age (Friberger; Bramwell and Hill).

While no definite figure can as yet be given as to the ranges that must be regarded as indicating pathological conditions of the arteries, a comparison of normal and pathological cases reported by the same investigator shows that, in accordance with the formula of Bramwell and Hill, the velocity tends to vary inversely as the percentage

[1] For original references, *cf.* Tigerstedt (Physiologie des Kreislaufes, 1893, 1st ed., p. 385) and Laubry (Mouget and Giroux (Arch. mal. du Cœur, 1922, **14**, 49, 97).

increase in volume per millimeter increases in pressure. Thus, the pulse velocity has been found to be greater in conditions of hypertension, arteriosclerosis, nephritis, etc. (Friberger; Laubry, Mougeot and Giroux; Bazett and Dreyer).

The velocity is decreased in aneurysms of the aorta and in cases of aortic stenosis. In Basedow's disease the velocity is often normal, but may be increased (Laubry, Mougeot and others). In aortic insufficiency the rate of transmission is said to be increased (Mougeot). Janowski has recently presented a formula by which the velocity coefficient may be readily determined from single pulse tracings. The formula reads:

$$C\,C\,P = \frac{P\,P^2}{T\,A\,P \times T\,D\,P}$$

in which $C\,C\,P$ represent the velocity coefficient, $P\,P^2$ the pulse pressure, $T\,A\,P$ the time of the ascending limb, and $T\,D\,P$ the time of the descending limb. Normal coefficients so calculated are said to range from 1.5 to 3.5.

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CHAPTER XII.

THE VENOUS PULSE OR PHLEBOGRAM.

If the cervical veins in the supraclavicular region are observed two distinct types of pulsation caused by their variable filling are evident. These are designated as the *respiratory and cardiac venous pulses.* With every inspiration, blood is aspirated into the thorax and the veins diminish in volume; with every expiration, the flow is impeded and the veins increase in size. If the breath is held during expiratory quiet, however, the cardiac variations normally superimposed upon the respiratory waves are more clearly discerned. During every systole of the ventricle, as gauged by the apex beat, the veins appear to collapse, thus giving rise to what has long been known as the "*negative pulse.*" This is distinguished from the pathological or "*positive venous pulse,*" which shows a systolic swelling of the veins. Unless otherwise qualified the term "venous pulse" designates the cardiac venous pulse, although the precautions have not always been taken to study its variations during apnea, hence a mixture of the two pulsations has often been obtained.

TECHNIC OF RECORDING VENOUS PULSE TRACINGS.

The cardiac variations in the jugular vein or jugular bulb can be studied in greater detail by taking graphic records of their volume changes. Attempts have been made to record the venous pulsations in the jugular vein directly, either by interposing the patient between a source of light and a photokymograph (Parkinson), or by transferring the pulsations of a vein to a light lever actuating a small mirror, from which, in turn, a beam of light is reflected (Ohm). These methods are, however, not universally applicable and offer no advantage over an indirect registration by transmission systems. The method employed by Parkinson is applicable only when strong pulsations exist in the external jugular vein. As this is relatively uncommon, especially in normal individuals, this procedure cannot be employed in a large number of instances. Furthermore, as the venous system with the auricle forms a manometer column of very low efficiency it is probable that the variations in volume and pressure are transmitted but imperfectly to the veins high in the neck. Consequently, records taken low down in the neck from the jugular bulb or subclavian vein much more closely agree with the pressure changes taking place in the large veins within the thorax. Ohm gives no data as to the effi-

ciency of his system. Calculations made by Straub indicate, however, that even when this system is constructed as lightly as possible the vibration frequency does not exceed 2.7 per second, making this apparatus very inferior to the worst form of graphic registration known. This fact, together with the difficulty in applying direct registration, makes it improbable that this method can be as efficient as indirect forms of registration.

Indirect transmission systems consist of a receiving cup connected by rubber tubing—preferably not more than 50 cm. in length—to a recording tambour writing on a kymograph or forming a part of an instrument known as a *polygraph*. Inasmuch as the accuracy of any tracing is largely determined by the efficiency of the recording systems, it is important to compare their efficiency with that of the optical segment capsule previously described (Figs. 59, 60).

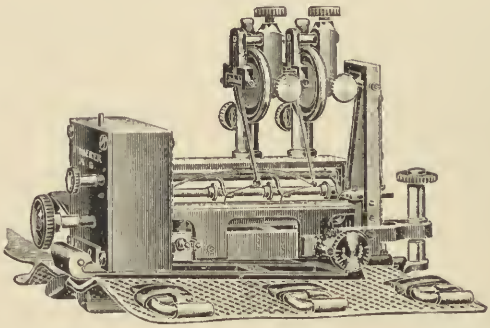

Fig. 73.—Jaquet polysphygmograph, recording radial pulse by wrist sphygmograph and carotid or jugular pulses through transmission tambours.

In polygraphs the recording tambours are so arranged that the levers of arterial and venous pressure recorders are placed closely together in order to enable them to record on a relatively narrow paper (Fig. 73). In order to render these systems sufficiently sensitive a considerable magnification of the lever is always necessary. In writing as they do, on horizontal surfaces, considerable friction between the writing point and the lever is, moreover, introduced. When, in addition, and contrary to all principles of good lever construction, a considerable weight is placed at the tip in order to enable these levers to record with ink, it can only follow that the instruments are inaccurate: (*a*) Because they have a very slow inherent frequency; (*b*) because the curves are modified by friction on the drum; and (*c*) because, being periodic, they introduce lever vibrations which are frequently interpreted as waves of the venous pulse. In testing the vibration frequency of a number of commonly used polygraphs the writer has obtained the following figures: Tambours of the Mackenzie ink polygraph have an inherent frequency of 4.5 per second, that of the Zimmer-

mann polygraph, 5.8 per second, while the Jaquet polygraph (Fig. 73) heads the list with a vibration frequency of 6.5 per second. Comparing these frequencies with that of 150 to 250 per second obtainable from the optical segment capsules, it is evident that they are recorders of relatively low efficiency.

The efficiency of such apparatus may also be tested by taking synchronous polygraph and optical tracings (Wiggers). When this is done the polygraphic record of the venous pulse shows the following inaccuracies: The form of the waves is more rounded, their amplitude and relative prominence may be incorrectly indicated, the time of rise and fall of the several waves is not accurate and, worst of all, these curves are often complicated by waves which do not exist in optically recorded pulse tracings.[1] Under abnormal conditions the contour of the waves is even more seriously affected. This is especially true in the case of the systolic waves. When tricuspid regurgitation occurs, for example, the contour of the waves is absolutely atypical in polygraphic curves (*cf.* Fig. 77). This is especially serious, inasmuch as large, rounded, systolic, polygraphic curves of this nature may be produced not only as a result of tricuspid regurgitation, but may be simulated whenever the aortic impact is unusually prominent (Wiggers and Niles). In spite of these deficiencies, however, the polygraphic recorders have proven very serviceable in establishing diagnoses.

While the nature of the recording apparatus is chiefly concerned in the accuracy of venous pulse tracings the character of the receiving cup is not entirely without significance. Usually an *open* receiving cup or funnel, 3 or 4 cm. in diameter, is applied over the jugular bulb or supraclavicular fossa with slight pressure, but in such a way that complete closure is made over the skin. A failure to do this results in pulse tracings which are inaccurate, owing to the fact that the individual waves drop before they should. To avoid this the receiving cup is sometimes closed either by means of rubber dam or a peritoneal membrane (Weber). To further facilitate the recording of pulse tracings small plaques of paper and cork have been glued to a surface and placed over the point of pulsations. There are arguments both in favor of and against such forms of closure (*cf.* Weber *vs.* Straub). It is certain that a stretched membrane, no matter what its character, which exerts a tension on the veins is undesirable and the intervention of a button or plaque can only operate to reduce the efficiency of a system. Inasmuch, however, as every system is really closed by means of the skin covering the opening of the receiving cup, nothing is lost and perfect closure is often gained by covering the receiving cup with a *very thin and absolutely unstretched rubber membrane,* a method that the author suggests and has found very useful.

[1] For curves illustrating such effects, *cf.* Wiggers: Jour. Am. Med. Assn., 1915, **64**, 1485.

The following technic is followed in taking venous pulse tracings by the transmission system: The subject lies for several minutes with the neck and head supported by a single pillow. The receiving tambour is applied snugly, but without undue pressure, to the *right supraclavicular fossa,* either over or to the right border of the sternocleidomastoid muscle. The effort should be made to relax the neck muscles by keeping the face directed forward or turning the head slightly toward the right—the involuntary tendency of the subject to turn the head to the left must be resisted.

When a place has been found where a satisfactory pulsation is obtained, another cup, also connected with a recording tambour or optical capsule, is firmly pressed over the carotid or subclavian area and, after marking the relative position of the two lever points, a tracing of these two pulses is simultaneously recorded, together with some form of time record. In place of the carotid pulse the radial pulse from a direct or transmission sphygmograph is sometimes used, or heart sounds are simultaneously recorded.

THE WAVES OF THE VENOUS PULSE, THEIR TIME RELATIONS AND INTERPRETATIONS.

Polygraphic Curves.—The cardiac venous pulse contains at least three, and occasionally four, waves for each heart cycle. Upon these, accidental wavelets or notches may be superimposed. Since the contours of the different waves are often not distinctive in polygraphic tracings, it is necessary to check them by comparison with the accompanying arterial curve. This, however, can be dispensed with in optical records after one has become familiar with the characteristic wave shapes. The checking is accomplished in the following manner (Fig. 74): One point of a pair of dividers is applied to the line indicating the starting position of the arterial lever x and the other to the rise of the primary wave of any arterial pulse, 1, 2, 3. Now, without changing the dividers, one point is applied similarly to the starting-point of the venous tracing x' and the wave cut by the other point determined, 1, 2, 3. *This is the second or systolic wave.* Its contour and prominence is variable. In case the radial pulse is used as a standard, 0.1 second is allowed for transmission time. Care should be taken to make all measurements between the line of points and the waves in the same horizontal line, so as to take into account the arcs of levers.

Nomenclature.—Various names have been applied to these waves. Following Mackenzie, the first wave is most commonly designated as the *a* wave, to denote its association with auricular systole. Since it is presystolic in relation to ventricular systole, it has also been called the presystolic or *p* wave (Bard).

The second wave is usually labeled the *c* wave, also after Mackenzie, to designate the fact that it owes its origin to a carotid impact. Since

it is systolic in time, it has been called the *systolic* or *s* wave (Fredericq, Bachmann, Ohm). Morrow speaks of it as the ventricular wave. Hering and Rihl have designated it as the ventricular valve wave or the *v k* wave, and Piper refers to it as the *K* wave.

The third wave is generally named, after Mackenzie, the ventricular or *v* wave. Morrow speaks of it as the *first onflow* wave. A number of investigators have noted that the ascending limb of this wave is divided by a notch or bend, and hence different names have been attached to these two portions. Thus, Bard speaks of a telesystolic and protodiastolic wave ($t + p$ wave), Wenckebach of an $i + v$ wave and Rihl of a v^s and v^d wave.

The fourth wave has been designated as the *h* wave by Hirschfelder, the *b* wave by Gibson and the stasis or *s* wave by Rihl.

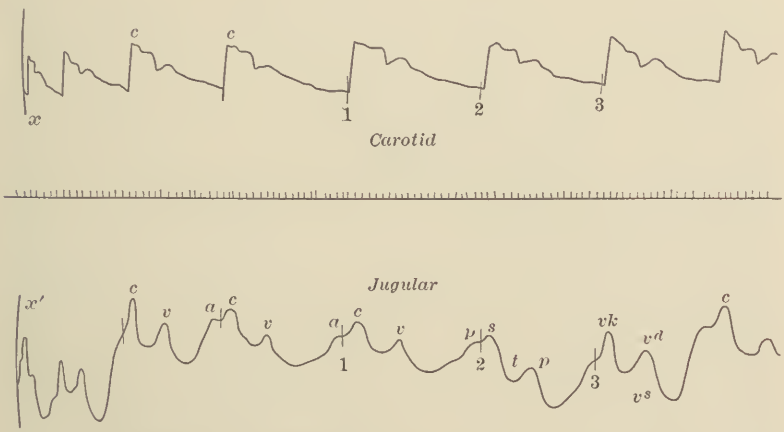

FIG. 74.—Simultaneous carotid and venous pulse tracings taken with a sensitive form of Lombard's tambour. x–x', relative position of writing points with arcs. On the record is illustrated the method of marking *c*-waves as well as the different terminologies found in the literature.

The Optically Recorded Venous Pulse.—Optically recorded tracings of the venous pulse have been reported by Edens, Veiel and Knapff, Weber, Van Zwaluwenburg and Hewlett, the writer and others. Illustrations are shown in Fig. 75. Like the graphically recorded pulse of the polygraph, they always contain three and sometimes four waves, corresponding to the *a*, *c*, *v* and *h* waves, already described. Time relations indicate that these are presystolic, systolic and diastolic in time.

The presystolic wave consists of a rise, *a–b*, and a fall, *b–c*. The systolic variations begin with a preliminary rise of pressure, during which a few vibrations are evident, *c–d*. Time relations show that this occurs during the isometric contraction phase. Absolutely synchronous with the elevation of the supraclavicular pulse at 3, the third

main wave *d–e* begins and is soon followed by a drop, *g*. This drop does not have a constant gradient, but is halted somewhere on the downstroke, *e. g.*, at *f*, at which point the gradient becomes less steep. The contour of this descending limb varies a great deal with the pressure at which the receiving tambour is applied as well as with the vigor of the arterial pulsations. When pressure is extremely light the waves drop abruptly and the curve may remain at an almost horizontal level during the remainder of systole (*cf.* Fig. 102).

The diastolic variations occur synchronously with the beginning of the incisura. They are initiated by a brief vibration, after which the pressure rises to its summit, *h*, and then declines. In sufficiently long cycles the pressure then either gradually elevates again until the abrupt

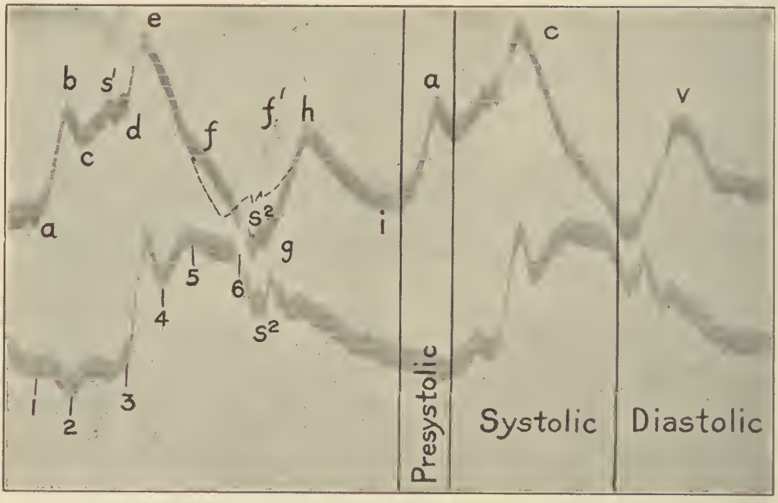

FIG. 75.—Supraclavicular venous pulse (upper) and subclavian pulse (lower) recorded by Frank's capsules.

rise of the succeeding auricular systole supervenes, or the gradual rise is interrupted by a definite coarse wave corresponding to the *h* wave of the venous pulse.

Time Relation of Waves.—The knowledge of the temporal relation of the various waves to other cardiodynamic events is fundamentally essential before an interpretation of the causes may be made, for, obviously, no dynamic process can be held accountable for any variation which does not occur isochronous with it. In looking over the voluminous literature bearing upon the time relations of the individual waves, one is astounded to find how great a diversity of opinion exists. Some of these discrepancies are now well known to be due to the use of inadequate apparatus; others must be referred to the inaccurate alignment of efficient recording systems; still others are due to

the fact that clear criteria for the beginning and end of certain cardiac events, such as ventricular systole and diastole, have not been clearly defined. In the succeeding lines it is possible to indicate only a few of the various conclusions reached by different investigators, and, finally, on the basis of critical interpretations, to formulate what seems, at the present stage of knowledge, the correct interpretation of these time relations. It is quite generally accepted, on the basis of myocardiographic studies, that the rise of the *a* wave begins with auricular systole; indeed, the synchronism reported by several investigators is incredibly exact. There is obviously a delay in the rise of this wave which becomes the greater the farther from the heart the pulse is recorded (Straub, 0.06 second; Van Zwaluwenburg and Agnew, 0.079–0.112 second; Wiggers, 0.06–0.092 second). The decline in the wave has generally been regarded as falling during auricular diastole, and this interpretation has been continued into some of the most recent literature (*cf.* Straub). Ewing was the first to point out, however, that auricular systole does not terminate at the crest of the wave, but continues almost throughout the fall. For reasons given in the first edition of this book, the author was inclined to question this interpretation, but as our conception of the nature of auricular systole became clearer (*cf.* page 67), it became evident that Ewing was quite right. Owing to the possibility that a short intersystolic interval may at times be present in man, it is impossible to determine accurately the end of systole as commonly defined.

The second wave undoubtedly begins to rise early in systole. How clearly it actually establishes the very beginning of systole has been much debated. Mackenzie regarded its rise as caused by and, hence, synchronous with the carotid impact. Bard, however, found that it preceded the carotid wave by 0.01 to 0.02 second, a fact given greater significance when Morrow subsequently showed that the waves were transmitted more slowly in the veins than in the arteries (1 to 3 meters as compared with 7 to 10 meters). Bachmann subsequently recorded curves in which this wave similarly preceded the carotid rise, but occurred synchronously with the apex rise attributed to ventricular systole. Eyster demonstrated that the first sound occurs on an average 0.03 to 0.07 second before the *c* wave rises, but may be coincident with it. A similar precedence of the *c* wave is reported by Fredericq, Rihl, Lian and others.

In 1911, Edens optically recorded the venous pulse with Frank's capsules and showed that the so-called systolic wave is made up of two portions, a first wave due to valve closure followed after an interval varying from 0.018 to 0.048 second by a true *c* wave. The first elevation occurs precisely at the onset of the first sound, whereas the true wave is somewhat delayed. Ohm simultaneously recorded the heart sounds and the venous pulse by his optically-recording gelatin capsules. These records also show that a short though uncalculated interval

elapses between the beginning of systole and the true *c* wave. The optical records reported by the writer in the first edition of this book are in exact agreement with these results (Fig. 75). They show that the true *c* wave rises an interval of 0.058 to 0.085 second after the onset of ventricular systole and that this period, moreover, corresponds to the isometric period calculated from the subclavian pulse. Precise agreement between the rise of the carotid wave and *c* wave of the optically recorded jugular pulse have since been further reported by Ohm and Weber, while Straub also points out that a short phase precedes the ejection of blood. The contrary findings of Veiel and Knapff will probably be explained by errors in alignment.

All investigators seem agreed that the drop of the third or *v* wave occurs synchronously with the opening of the tricuspid valves. The summit is, therefore, commonly regarded as approximately coinciding with the onset of diastole. Thus, Rautenberg, by comparing esophageal and venous tracings, came to the conclusion that the entire rise was systolic and the summit marked the beginning of diastole. On the other hand, Wenckebach believed that the foot of the rise was synchronous with the diastolic onset. According to a more recent statement by Mackenzie, Gottwalt, Knoll and Hering, the rise begins during the end of systole and continues into early diastole. According to this view, the beginning of diastole occurs somewhere on the ascent of this wave and is often marked by a notch or jog. This view is substantiated by optical tracings and simultaneous records of sounds and waves. Thus, Eyster found that the second heart sound begins on the average a few hundredths of a second after the beginning of the *v* wave, although this sound has been observed as much as 0.045 second before and 0.15 second after its rise. The records taken by Edens, Straub, Weber and the writer with Frank's capsules, as well as those of Ohm taken with gelatin membranes, show that the third wave is essentially, and often entirely, a diastolic one, provided we take the closure of the semilunar valves as establishing the end of systole and the beginning of diastole (Fig. 75).

It is obvious that these differences of opinion have resulted from various definitions of *systole* rather than from essential differences in records. With the belief that closure of the semilunar valves and opening of the tricuspids occur essentially simultaneously, the belief that the summit of the *v* wave marks the end of systole also followed. As we now know that a considerable interval elapses between the end of systole and the opening of the *A–V* valves (*cf.* page 99), it is necessary to more exactly locate the end of systole, viz., at the beginning of the aortic incisura or second heart sound. When this is done it usually follows that most if not all of the ascending limb occurs during diastole.

The fourth wave when present is distinctly diastolic in time. Hirschfelder, Thayer and Gibson all related it to the third heart sound (see

page 321). This is confirmed to a certain extent by the work of Eyster, who found that the third sound precedes the beginning of this wave by a few hundredths of a second. This writer also corroborates the work of Einthoven, however, showing that the two are not necessarily associated, since a sound may occur without evidence of a wave, and *vice versa.*

The Physical Nature of the Venous Pulsations.—Before we essay to interpret the various waves of the venous pulse, it is essential to have a clear mental picture as to what we are actually recording. The cervical veins in a sense represent manometer tubes connected with the auricle, and consequently it may be supposed that they give an index of pressure variations occurring within the auricle—a view originally advanced by Fredericq. Most investigators, however, following the suggestion of Wenckebach, believe that the pressure variations are only poorly transmitted through the readily distensible veins, and that the venous pulse represents essentially changes in volume due to varying outflow of blood toward the heart, *i. e.*, that it is a *phlebogram* rather than a pressure curve. This interpretation cannot be questioned, but, as Straub justly points out, it is difficult to comprehend how changes in venous flow can be occasioned except through variations of pressure at their entrance into the auricle. Consequently, while we might insist, for academic reasons, that venous pulse tracings are essentially volume curves of the veins, it must also be admitted that these variations are essentially determined by minute variations of pressure.

It may be pointed out, moreover, that this discussion is entirely dissociated from the question whether the venous pulse accurately corresponds to pressure variations within the auricle. A number of factors may conceivably alter the rate of flow which determines the contour and time relations of the individual waves. Among these may be cited: (1) The varying degree of intrathoracic negative pressure, which alters not only with the phases of inspiration and expiration but also with different phases of the cardiac cycle; (2) changes in position of the heart, which, on one hand, may act to occlude the orifices, or, on the other hand, to open them up; (3) a varying traction, which the moving part may exert on the large veins, thus mechanically altering their capacity and diameter. In addition to these, it is not certain that all the waves recorded have their origin in the veins or auricle; on the contrary, impacts from the large underlying arteries upon the veins, or from the aorta on the auricle itself, may add extraneous waves. Since these influences vary markedly in different animals and men, it is not surprising that different types of results have been obtained and that the applicability of such results to the venous pulse in man have been variously interpreted.

The Interpretation of Waves.—Two essentially different conceptions as to the cause of the presystolic rise of the *a* wave have been

formulated: (1) That at the beginning of auricular systole the fibers around the venous ostia contract so as to partially or completely shut off the flow of blood from the auricle, thereby causing a swelling of the veins (Keith); (2) that the resistance to venous flow is caused by and is proportional to the increase of pressure within the auricle during auricular systole. That the latter mechanism is the correct one is indicated by the optical records obtained by Piper, Straub, Wiggers and others, which show that the *a* wave, though belated, rises and falls fairly synchronously with the auricular wave of the intra-auricular pressure tracings. Other investigators (notably Weber) find, however, no correspondence and point out that considerable variations may occur in venous tracings taken from different regions. The author is of the opinion that such differences undoubtedly depend on the degree of auricular filling. Experiments carried out under conditions in which the veins are well filled and consequently incapable of much greater distention show a close correspondence; when, however, the veins are relatively empty they become much poorer manometer systems and consequently their volume changes do not follow the intra-auricular pressure. In such cases the velocity with which pressure variations are transmitted backward and affect the flow in the veins varies at every moment. It is difficult to determine whether the rise of the *a* wave in man corresponds fairly exactly with intra-auricular pressure changes. In normal individuals with poorly filled veins the time relations must remain doubtful, as also the relation during deep inspiration. When, however, the veins are well filled, as is usually the case in the lying position, and when a definite pulsation is visible, it is probable that if taken low in the neck the *a* waves correspond fairly accurately with intra-auricular pressure changes.

The fall of the *a* wave has been variously interpreted as due to: (*a*) Auricular diastole; (*b*) ventricular systole drawing down the floor and thus enlarging the capacity of the right auricle; (*c*) a decrease in intrathoracic pressure at the onset of ventricular systole. All of these interpretations are now thrown out of consideration by time relations, which make it necessary to explain the pressure decline during continued auricular systole. The explanation of Ewing, that it is due to a rebound of the blood column causing a returned flow, does not appear probable, since it has now been established that a similar fall of pressure occurs simultaneously in the right auricle (*cf.* page 89). The author interprets this fall of pressure as due to the progressive elimination of fractionate contractions from the auricular contraction process (*cf.* page 70).

While there is a stagnation of blood during the rise of the *a* wave there is an actual auricle-ward flow during the decline of pressure (Burton-Opitz), thus permitting us, on the basis of the venous pulse alone, to make a fairly accurate determination of the dynamic and inflow phases of auricular systole (*cf.* page 100).

Most investigators now admit that in accurate tracings a small notch, a short halt or a series of vibrations occur between the end of the presystolic and the rise of the systolic wave (Fig. 75, *c–d*). Sometimes the curve moves upward slightly and at other times downward during this interval. This period of the heart has been interpreted as due to: (*a*) An intersystolic interval (Bard), and (*b*) to a presystolic closure of the *A–V* valves (Hering). The fact that accurate time relations show this phase to occur during the isometric rise of pressure precludes these interpretations. During the isometric phase of contraction several events occur which tend to cause a slight upward movement of the venous pulse waves. Among them are: (*a*) Closure of the *A–V* valves, and (*b*) bulging of the valves by virtue of the intraventricular pressure rise. On the other hand, this may be counterbalanced or overbalanced by the effect of: (*a*) A contraction of the papillary muscles drawing down the *A–V* valves, and (*b*) the descent of the *A–V* floor during ventricular contraction. Under these opposing influences the curves may remain horizontal or directed upward or downward, depending upon the predominant influence. Always, however, we find some evidence of vibrations, due to first heart sounds superimposed upon the curves at this point. In spite of some evidence to the contrary, which must be attributed to technical errors, the main wave rises synchronously with that of the neighboring arterial pulse. This fact supports the idea that the systolic wave is due to an impact from some underlying artery (Mackenzie). The chief argument which is used, as opposed to such an explanation, consists in the observation that a positive systolic wave also occurs within the auricle.

The writer has made an effort to trace carefully the transformation of the intra-auricular pressure curve into the venous pulse as commonly recorded. This work was done partly in association with Frank and Brömser, in Munich, and partly independently through subsequent experiments in Cornell Medical College. The facts may be briefly outlined in connection with the diagram of Fig. 76:

1. If the intra-auricular pressure from an animal with an active heart is recorded by a sensitive optically recording manometer of adequate efficiency we find, similar to the results of Straub and Piper, that the pressure variations in the auricle are composed of the following typical series of waves (Fig. 76, *I;* also Fig. 22, *B*).

A rise and fall, *a, b, c,* synchronous with the dynamic and inflow phases of auricular systole.

A sharp, positive rise and negative fall, *c, d, e,* apparently associated with valve closure and downward movement of the auricular floor.

A slow stasis rise continuing throughout systole, *e, f,* and marked at the closure of the semilunars by a notch, *f.*

A diastolic rise, *f, g.*

A diastolic drop, *g,* due to the opening of the tricuspid valves.

A mid-diastolic oscillation, *h,* when the heart is slow.

2. If a jugular vein is tied and the pressure within is recorded low in the neck with the same optical manometer the following series of changes are found (Fig. 76, *II*).

A rise and fall, *a*, *b*, *c*, due to auricular systole. This rise occurs a few hundredths of a second later than the rise in the auricle, but is often preceded by a negative depression which is apparently accounted for by a slight traction of the contracting auricle on the veins.

A small notch *c*, *d*, corresponding to a similar rise in the auricle, but not followed by the sharp drop, *d*, *e*, since it is cut short by a prominent elevation, *s*, apparently due to a systolic impact from some intrathoracic artery.

A late systolic rise, to *f*.

A diastolic rise, *f*, *g*.

A diastolic depression, *g*.

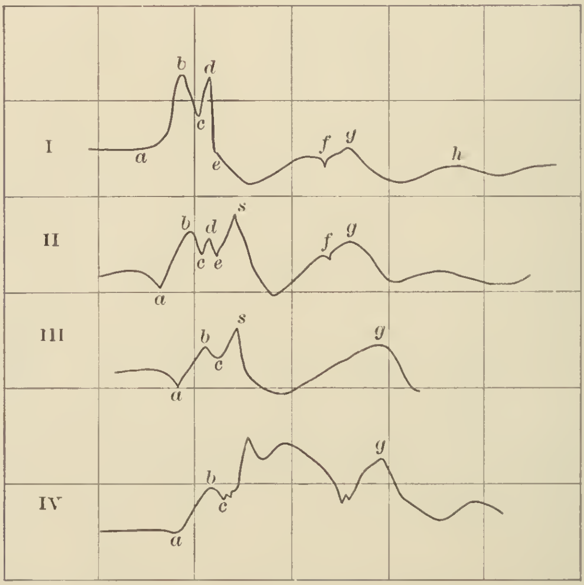

FIG. 76.—Four curves showing transition of right auricular pulse to supraclavicular venous pulse. *I*, pressure changes in right auricle; *II*, pressure changes in extra-thoracic veins; *III*, volume changes of neck vein; *IV*, supraclavicular pulse taken with tambour.

To sum up, the pressure waves have changed to the extent that the steep fall, *d*, *e*, is largely replaced by a second positive wave, *s*, and that the stasis rise during systole starts later.

3. If the jugular vein low in the neck is dissected free, but not tied, so that blood flows from the periphery, and the variations in venous volume are directly recorded by methods of unquestionable accuracy, then the three main waves persist; but all evidence of the variations due

to valve closure or movements of the auricular floor, *c*, *d*, *e*, have vanished—probably they have been damped out by the presence of valves or the onflowing blood (Fig. 76, *III*).

4. If a supraclavicular tracing is taken as in man, by placing a small tambour over the skin of the venous region, the curve again contains three waves, but the systolic wave assumes greater prominence and gives distinct evidence of the detailed contour of a central arterial wave. The *v* wave becomes almost entirely a diastolic affair (Fig. 76, *IV*).

To summarize we may say: (1) There exists in the right auricle a small systolic wave due to the movement of valves or the auriculo-ventricular floor; (2) there exists in the central veins (occasionally in the auricle) another distinct wave, due to an intrathoracic impact; (3) the latter is and the former is not transmitted to the veins of the neck; (4) it is difficult to record either of these systolic vibrations when a small tambour simultaneously covers an arterial area, for then the period of systole is obscured by a direct arterial impact.

Such experiments indicate that the venous pulse does not follow intra-auricular pressure changes *during ventricular systole.* During this period of the cardiac cycle the venous curve mainly falls, while the intra-auricular curve mainly rises. This is also shown in records published by Van Zwaluwenburg and Agnew, Piper, Straub and others. Such observations do not indicate that the rise of intra-auricular pressure during ventricular systole in no way affects the venous pulse tracings. In many tracings, such as are shown in Fig. 75, it may halt the rate of decline, as at *f*, or if the rise occurs somewhat more rapidly it may terminate the systolic drop, as shown in the dotted lines. In this case the curve rises distinctly at the end of systole, S^2, and the systolic rise merges into the diastolic rise of the *v* waves. It is interrupted then by a small notch, S^2. When arterial impacts are small, when a very light pressure is used or when the venous volume is large, it is not uncommon to find a gradually increasing curve during the greater part of systole. In inspecting 480 optical records obtained during class experiments, I have frequently seen curves that after the first 0.02 or 0.03 second of a systolic ejection looked almost precisely like pressure curves taken from the right auricle in animals. Such records are, however, the exceptions and not the rule.

It is generally supposed that the rise of the *v* wave is but a continuation of the stasis curve occurring during auricular systole within the auricles. Its more pronounced character at this time is attributed to the fact that the auricles have become overdistended and now dam their blood back into the veins (Mackenzie, Hering, Rautenberg, Straub). The facts that the rise occurs with such unusual steepness and suddenness, often at the moment that diastole begins, and that no sudden change in gradient is usually seen in intra-auricular pressure curves from the right auricle, have suggested that this rise may

be mechanically assisted by certain diastolic events occurring, to be precise, during the isometric relaxation phase of the heart (Wenckebach, Eden, Rihl). The nature of these mechanical factors have not always been clearly stated. They have been attributed to an ascent of the cardiac base (Rihl, Wenckebach) or a transmitted effect resulting in some way from the bulging of the semilunar valves and their closure. That these explanations are inadequate is shown by the fact that such effects should simultaneously increase intra-auricular pressures as well. The idea that it may be due to a relaxation of the pull exerted by the contracting ventricle on the vein, or that it may be occasioned by an increased intrathoracic pressure when a backflow of blood occurs during diastole into the large thoracic artery, are also not satisfactory as explanations. If mechanical factors contribute it can only be said that their nature has not been clearly defined.

The sudden fall of the *v* wave is usually assumed to indicate the moment when the tricuspid valves open and blood flows from auricle to ventricle. Comparison of the right auricular and venous pressure curves indicates that this assumption is correct.

Very little is known as to the cause of the second diastolic or *h* wave. The suggestion that it is due to a sudden floating together of the *A–V* valves at the end of the rapid inflow and beginning of diastasis (Hirschfelder) does not accord with the following facts: (1) The wave is not necessarily associated with the third sound when the latter is recorded (Einthoven, Eyster); (2) the valves do not snap together sharply at this time but gradually float together throughout diastole (Dean); (3) several such waves may occur in long diastolic intervals during auricular fibrillation which would necessitate the assumption of a "flip-flop" repeating mechanism (Niles and Wiggers).

CLINICAL ASPECTS OF THE VENOUS PULSE.

Significance of Changes in Contour of the Systolic Wave.—In spite of the fact that the venous pulse, as recorded from man, probably follows intra-auricular pressure changes only during the interval extending from the beginning of the *v* wave drop to the beginning of the next ventricular systole, attempts have been made to utilize changes in the contour of the systolic wave as an index of changes in intra-auricular pressure. On the basis of polygraphic as well as optical tracings it has been suggested that the premature termination of the systolic drop and the corresponding earlier rise of the *v* wave (*i. e.*, in systole instead of at the beginning of diastole) may offer a means of determining whether a stasis or increased venous return exists (Wenckebach, Ohm, Weber, Straub). As stated by Straub, the time when the systolic collapse terminates is probably determined by: (*a*) The capacity of the right auricle and entering veins; (*b*) the volume retained in the auricle during auricular systole; (*c*) the volume of inflow during

diastole. When any of these factors are increased beyond normal the systolic drop is overbalanced by the rise of pressure within the auricle and consequently terminates sooner. The progressive changes that may be found in optical as well as in polygraphic tracings are illustrated in Fig. 77.

The systolic or *c* wave in optical tracings is normally very prominent; in polygraphic tracings it may be scarcely indicated. Its chief characteristic is that it *falls during the major part of systole* (Fig. 77, *I*). The relative time of the termination of this fall indicates in some fashion the degree of stasis in the right auricle. If the stasis is greater than normal the rise occurs during the end of systole. Further stasis causes the wave to remain high, as shown in Fig. 77, *III*. In such

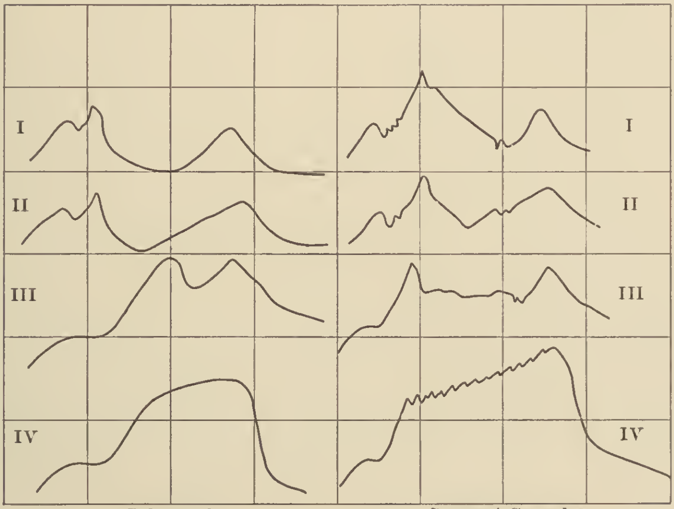

FIG. 77.—Comparative diagrams illustrating the effect of a consecutive increase in stasis, *I*, *II*, *III*, and of regurgitation, *IV*, on the venous pulse curves as recorded by optical apparatus and polygraph tambours.

cases the systolic or *c* wave and the diastolic or *v* wave are always distinctly separated by a notch in optical tracings. Aided by lever throw, these notches may become very deep in polygraph curves and give the effect of a bifurcated wave.

The diagnostic importance of such changes is, however, open to question. Weber particularly maintains that it is always an early sign of circulatory stasis, reporting that in 50 normal cases it was never observed, while in 399 out of 400 compensated hearts it was always present. Without denying the possibility of its occurrence in venous stasis, Straub maintains, however, that it may occur under physiological conditions. In 300 venous pulse tracings from normal men examined in regard to this point, the author has found that in 89

individuals the wave begins to rise from 0.01 to 0.04 second before the second heart sound.

The contour of the systolic wave is altered during tricuspid insufficiency. As shown in curves *IV* of Fig. 77, the venous pulse rises throughout systole and the systolic and diastolic waves merge into one with a broad plateau. In such cases the optical records indicate clearly the vibrations of the murmur accompanying the regurgitation. Since in this form of pulse the systolic waves are exceedingly conspicuous, it has been designated the "ventricular type" of venous pulse (Mackenzie).

Optical tracings of these pulsations have been reported by Ohm and the writer. One of the curves shown in Fig. 173, taken from a case of auricular fibrillation, illustrates that when the heart beats are irregular, different types of waves may follow each other. Thus, in the group labeled *I* a distinct impact or *c* wave occurs, which is followed somewhat prematurely by a rise of the *v* wave, indicating stasis. In groups labeled *II* we have the entire systole filled by an ascending or horizontal plateau, in which vibrations due to an accompanying murmur are vaguely discernible. Here the *c* and *v* waves are merged.

A prominent systolic wave may also occur when auricle and ventricle contract simultaneously. This may occur occasionally or for considerable intervals in paroxysmal tachycardia (Mackenzie). In such an event a sustained top is not found, however, but the curves resemble a large wave. An example of such curve is shown in Fig. 144 (Hewlett).

A sharp, distinct systolic wave may be entirely lacking when an ineffective systole occurs, that is, one that fails to open the semilunar valves and sends no pulse to the arteries. In such cases the registration of heart sounds alone will determine the presence of a ventricular systole.[1]

The Significance of the Presystolic Wave.—The auricular wave is of importance in establishing the existence or absence of auricular contractions. If a distinct wave is present from 0.08 to 0.2 second, before the curve rises the assumption is generally made that it represents the presence of a systolic wave. If the interval is longer it should be regarded suspiciously. Occasionally, even in optical records, it becomes exceedingly difficult to determine whether a certain wave is due to auricular systole.

Again, it not infrequently happens that the *a* wave is entirely absent in records taken with the breath held (Edens). This probably occurs when the contractions are weak or when the venous pressure is unusually low. In such cases a regular rhythm warrants a closer investigation into the existence of the *a* waves, for their absence throughout a record usually occurs only with an irregular ventricular rhythm.

[1] For a consideration of systolic wave-types in auricular fibrillation, *cf.* page 486; also Niles and Wiggers: Jour. Exp. Med., 1917, **25**, 1.

Even in cases with irregular hearts, however, the *a* waves may apparently be absent when they occur synchronously with carotid systoles or during the *v* waves. According to Lewis, we may suspect such a coincidence of the *a* and *v* waves when the *v* wave projects distinctly into diastole. This criterion is of doubtful value. Many of the interpretations of synchronous *a* and *c* or *a* and *v* waves should be questioned unless verified by other means. True *a* waves are, of course, absent when the auricle is extremely distended or in a state of fibrillary contraction.

The *a* wave may determine the abnormal sequence or the excessive recurrence of auricular contractions. In deciding that the presence of certain waves indicates an excessive rate of auricular contraction, it is necessary that all the other possible causes of such waves be excluded. The *h* waves may recur so as to be equidistant from two regular *a* waves and, hence, mistaken for extracontractions of the auricle. If such a wave is less prominent than the recognized *a* waves, and if no other evidence of arrhythmia is found, it is probably an *h* wave. Again, *a* waves may be confused with *v* waves. Lewis proposes to differentiate by determining whether the drop comes after the dicrotic notch. This method, however, is of little value, especially in polygraphic tracings, for the *v* wave begins to fall after the dicrotic notch. Furthermore, most of the tambours on the polygraphs record no dicrotic notch but merely an inherent after-vibration (*cf.* page 222). When the heart is very irregular the curve may be further complicated by the fact that ineffective ventricular systoles cause small waves in the auricle, which simulate those due to auricular contraction. Thus, it is very questionable whether all the small waves found in curves of auricular flutter can be referred to contraction of the auricle and its tempo so determined (*cf.* Fig. 156). Furthermore, in cases undoubtedly established as auricular fibrillation, presystolic waves closely resembling *a* waves are not infrequently found (Niles and Wiggers).

Significance of Time Relations.—Adopting the conclusions reached as to the significance of the various waves, we may state the importance of time relations. In a foregoing chapter it was shown that the duration of the isometric contraction phase, the ejection phase, as well as the protodiastolic phase of the human heart cycle, can be calculated from the central arterial pulse. Similarly, certain phases of diastole may be calculated with approximate accuracy from the optical venous pulse curves. Thus, after the protodiastolic phase, the ventricle continues to relax isometrically until the *A–V* valves open. Regardless, therefore, of whether the rise of the *v* wave does or does not represent a true stasis curve, the interval extending from the bottom of the incisura of the arterial pulse to the beginning of the *v* wave drop (Fig. 75, S^2–*h*) represents the phase of isometric relaxation. Similarly, the duration of the drop *h–i* indicates approximately the phase of rapid inflow. The interval between the bottom of this fall and the subsequent ele-

vation of the a wave (if any) gives the interval of diastasis. On the a wave we may calculate: (1) The dynamic phase of systole by the rise, and (2) the inflow phase of systole (approximately) by the drop, b–c. While not precisely correct, no serious error is made if the interval A–C is considered to be the duration of total auricular systole.

It is evident, therefore, that by the aid of combined venous and arterial tracings, recorded by optical means, it is possible to subdivide, with a fair degree of accuracy, the cardiac cycle into its consecutive phases.[1]

The a–c Interval.—The time interval from the rise of the presystolic or a wave to the systolic or c wave is called the a–c interval. It is generally regarded as giving an estimate of the time interval between auricular and ventricular contraction (As–Vs interval), and so permits a determination of the conduction time from the auricle to ventricle. This interval is slightly longer than the P–R interval of the electrocardiogram, which may be due to the fact that the a and c waves are transmitted with irregular velocity to the neck or to the fact that the records represent different phenomena (*cf.* page 285, Electrocardiogram).

According to Lewis, it has been established by electrocardiographic studies that whenever this interval is longer than 0.3 second it may be assumed to be due to an increase in the conduction time.

The idea that the a–c interval may be used as a criterion of the conduction time presupposes, first of all, that the venous a wave and the arterial c wave are conducted to the neck at a constant velocity. It is evident from optical tracings that this is not so, especially in cases of irregularity in which the isometric period of the ventricle varies and the rate of arterial transmission is slower. Passing this source of error by, however, one may examine what this interval really represents. It embraces: (a) The systole of the auricle; (b) the intersystolic interval; (c) the period of rising tension in the ventricle; (d) the transmission time of the arterial pulse to the neck.

It was formerly assumed that the same impulse that set off the auricle passed on and stimulated the ventricle. Hence, it was reasoned that if we assumed the systole of the auricle, the period of rising tension and the transmission time to be equal—in itself somewhat daring in the case of irregularities in which experiments show them to be prolonged—then the a–c interval represents the time taken for the impulse to be conducted from auricle to ventricle.

Recent work, however, has shown it to be improbable that the impulse is conducted to the ventricle *via* the auricle,[2] but directly from the S–A node, hence the As–Vs interval is not necessarily related to the sinoventricular conduction period.

[1] For duration of these phases, *cf.* Chapter III, page 100.

[2] The term "auricle" is here used not as synonymous with "atrium," but as "*the main body of the contracting auricle.*"

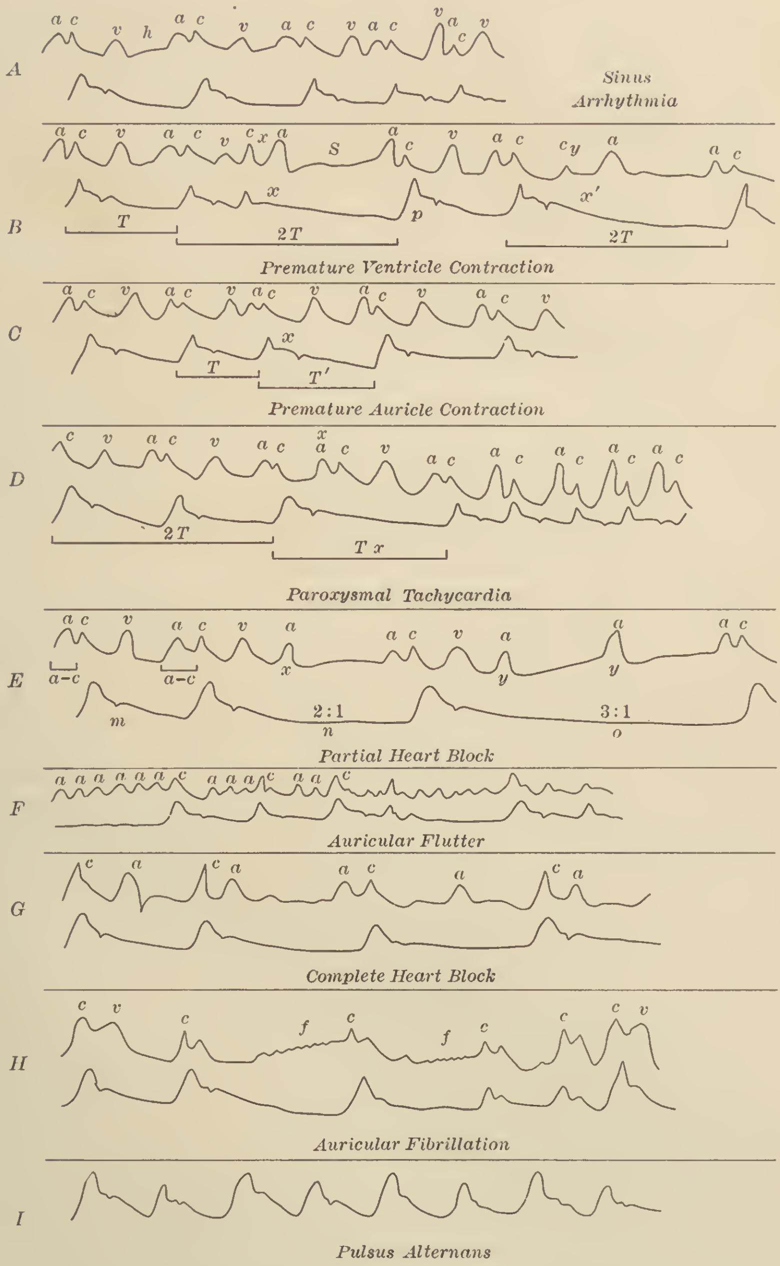

Fig. 78.—Scheme showing the effect of various forms of arrhythmias on the arterial and venous pulses. For description of the arterial pulses, *cf.* page 211; of venous pulses, page 240.

It must be admitted that for many reasons the *a–c* interval cannot be implicitly regarded as an index of sino-ventricular conduction time. That it does correspond so well with the electrocardiogram *P–R* intervals is, in fact, extremely remarkable.

Cardiac Arrhythmias.—As tracings of the venous pulse by polygraph tambours are of service in the diagnosis of certain cardiac irregularities, the more typical records found in some of the more common forms of irregularity may be briefly discussed in relation to the curves shown in Fig. 78.

A more detailed exposition of the various forms of irregularity will be found in a subsequent chapter.

A. Sinus Arrhythmia.—The venous pulse is usually characterized by a regular sequence of the *a*, *c*, *v* waves and a normal *a–c* interval (0.1 to 0.2 second). The irregularity consists in the early or late occurrence of each group. Individual variations may arise in which the length of cycles varies markedly. Thus, in the long cycles an *h* wave may occur while in the shorter ones the *v* wave may be combined with the next *a* wave. In extreme cases the *a–c* interval may also vary, but it cannot be definitely accepted that this represents an altered conduction time.

B. Premature Ventricular Contraction.—The venous pulse is characterized by a premature *c* wave as at *x*. This is followed by an auricular contraction, *a*. Since this stimulus finds the ventricle in its refractory phase, it is followed by no *c–v* complex (*cf.* Fig. 147). For this is substituted a stasis rise, *S*, which fills the compensatory period. The premature systole may occur so early, *y*, that it replaces the *v* wave. Such a systole is usually so weak, however, that the semilunar valves fail to open and a wave fails to appear in the arterial tracing taken from the wrist. It may, in fact, happen that no extra *c* wave appears in the venous pulse, the presence of the extracontraction being then recognized only by the heart sounds in optical tracings.

C. Premature Auricular Contraction.—The venous tracing is characterized by a normal *a*, *c*, *v* sequence, for an entire *a*, *c*, *v* group occurs prematurely as at *x*. The *a–c* interval is increased, due, perhaps, to the changed sino-ventricular transmission time.

D. Paroxysmal Tachycardia.—The venous curve shows, previous to onset, one or several auricular extrasystoles, *i. e.*, premature *a*, *c*, *v* wave groups, followed by an interval with a stasis rise. At the onset of tachycardia the *a*, *c*, *v* sequence is disturbed only by the fact that the *v* wave becomes merged with the succeeding auricular contraction.

E. Incomplete Heart-block.—The earliest stages are said to be indicated by a lengthening of the *a–c* interval alone. Such curves should be corroborated, however, by other evidence before diagnosing an impaired conductivity. Similarly, impaired conductivity between sinus and ventricle may occur with an *a–c* interval entirely normal. The diagnosis may be made, however, when a long *a–c* interval or a

progressively increasing interval is followed occasionally or regularly by a dropped arterial beat. In such cases, illustrated at *x* and *y*, the *a* wave recurs regularly but is not followed by the *c–v* complexes.

F. Auricular Flutter.—The venous pulse, when the arterial rate is slow, shows a rapid succession of small *a* waves, which are occasionally interrupted by waves of ventricular origin (*cf.* also Fig. 156). When the ventricle beats rapidly, however, and tricuspid regurgitation supervenes, all evidence of auricular contraction may be obscured and the ventricular form of venous pulse alone predominate. In such cases the venous pulse is not diagnostic.

G. Complete Heart-block.—The venous pulse shows a regular succession of *a* waves, interrupted at irregular intervals by *c* and *v* waves of ventricular origin. These groups fall between the *a* waves or are superimposed upon them.

H. Auricular Fibrillation.—The venous pulse is characterized by an entire absence of *a* waves and the presence of ventricular *c–v* complexes. These have a varying conformation and recur very irregularly but at a rather rapid rate. Between these systolic groups are long stasis periods, upon which small undulations attributed to auricular fibrillations are evident. Other smaller waves, due, perhaps, to ineffective systoles of the ventricles and other causes as yet unknown, are common (*cf.* also Fig. 173).

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CHAPTER XIII.

THE ESOPHAGEAL PULSE AND THE ESOPHAGRAM.

If an esophagoscope is inserted into the esophagus, pulsations are visible in two places. The upper pulsations, which are the weaker, are seen at about the level of the tracheal bifurcation, or about 26 to 30 cm. from the teeth (Rautenberg). The lower pulsations, which are more vigorous, occur somewhat lower down, 32 to 36 cm. from the teeth (Rautenberg). A study of the anatomical relations shows that in this region the left auricle is in direct contact with the esophagus for a distance of 5 to 6 cm., hence the pulsations are evidently transmitted directly from it to the esophagus.

Registration.—The idea of obtaining esophagrams, as the records may be termed, occurred first to Luciani and later to Fredericq and his pupils, who employed the method in animals. To Rautenberg and Minkowski, however, we owe the clinical application of the method.

To obtain an esophagram the following technic is usually followed: After cocainization of the pharynx a lubricated rubber tube, about 5 mm. in diameter and 75 cm. in length, which is equipped below with a small soft rubber bag, is swallowed to a distance of about 38 cm. The bag is then gently inflated and gradually drawn out either until a distinct pulsation is obtained in the tambour with which it is connected, or until the heart sounds heard through a connected stethoscope become loudest. The tendency to swallow saliva must be counteracted by suitable means, either by allowing it to drip into a receptacle or by employing one of the various drying appliances used by dentists for similar purposes. The records are preferably taken in the sitting posture, but if it is necessary to recline the lateral or abdominal position should be assumed.

Nature and Time Relations of the Records.—As can readily be understood, the records necessarily differ according to the part of the esophagus from which they are recorded (Young and Hewlett, Edens). With the most exact placement over the left auricular area, three waves, regarded as similar in character to those obtained from the venous pulse, are recorded (Fig. 79). They have been designated as the *As*, *Vs* and *D* waves by Rautenberg. As has been pointed out by Young and Hewlett, as well as by Edens, however, a distinct *As* wave is not always present, but in the upper and lower portions of the auricular area it is replaced by a negative drop. The time relations of these waves have been compared with the waves of the jugular pulse in a previous section

of this book. It is only necessary to repeat that they precede the corresponding jugular pulse waves by irregular intervals. Their exact relations to the waves of the electrocardiogram have been established by Rautenberg, Kahn and more recently by Benjamins. The *As* wave rises with 0.015 second after the rise of the *P* wave and the fall continues until the *Q* depression of the electrocardiogram. The rise of the *R* wave also precedes the mechanical elevation *Vs* by a similar interval. The *D* wave drops a distinct interval after the end of the *T* wave.

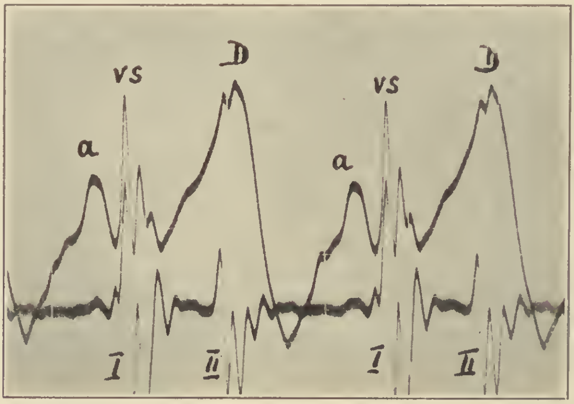

FIG. 79.—Esophagram and heart sounds recorded with segment capsules. *a*, auricular wave; *v s*, systolic wave; *D*, diastolic peak. Lower records show first and second sounds. (After Edens.)

Interpretation of the Esophagram.—The interpretation of the esophagram involves the question as to what form of cardial activity is actually transmitted to the esophagus. The anatomical proximity of the left auricle to the esophagus has led to the natural inference that the intra-auricular pressure variations are transmitted through the elastic walls of the auricle and esophagus. Van Zwaluwenburg and Agnew have supported this view by showing that the waves in the auricle and those recorded from the esophagus by optical apparatus correspond exactly. This fact, however, does not conclusively indicate that the two sets of waves are due to exactly the same influence. It has been suggested that the changing position of the auricle during its systole and diastole, as well as the traction influence of the ventricular systole, must directly modify the intraesophageal pressure. Attention has likewise been called to the effect of cardiopneumatic variations in intrathoracic pressure upon the esophagram. Luciani as early as 1877 reported that the esophagram taken from an intact thorax differed essentially from one recorded when the thorax was opened. Too much significance, however, should not be attached to such observations, for not only is a great risk incurred of directly altering the position of the sound, but, in addition, the entire circulation phenomena are known to

change when the chest is opened so that one should expect a difference in the esophagram apart from that caused by negative pressure. The results of Meltzer and Auer lead us to believe that the importance of the part played by cardiopneumatic phenomena is doubtful, since they have shown that the negative pressure variations within the thorax were very poorly transmitted to the posterior mediastinal area below the bifurcation of the trachea.

In interpreting the esophagram as an index of left auricular activity, it should be remembered that it represents a combined influence of auricular position change and intra-auricular pressure phenomena. For this reason different types of curves may be obtained from different regions of the esophagus. The *As* wave when present is undoubtedly associated with a contraction of the auricle and so is presumably caused by its central bulging as the pressure rises. When, instead of this wave, a negative drop appears it is probably because the contracting auricle draws away from the esophagus in the place where the record is taken. The *Vs* wave, attributed by Rautenberg to a change in the length of the heart as a result of ventricular systole, is shown by optical methods (Edens) to be a more complicated phenomenon. It seems very probable from the nature of the oscillations present that the vibrations of the mitral valves are concerned. Following these vibrations the pressure rises, due to stasis, very much as in the intra-auricular pressure curve. As at the opening of the tricuspid valves the auricular pressure rapidly falls and the position of the heart changes as well, the curve drops quickly. It is evident that with proper allowances for a possible predominating influence of cardiac movement the esophagram follows the changes in the intra-auricular pressure closely (Edens, Van Zwaluwenburg and Agnew).

CLINICAL VALUE OF THE ESOPHAGRAM.

The ways in which the esophagram has been considered useful in clinical cases may be briefly enumerated:

1. It establishes the existence of auricular activity, but in this capacity it merely supplements information gained from records of the jugular pulse.

2. It gives evidence of dissociated activity of the two auricles. Edens published a rare case in which the left auricle was apparently paralyzed, due to distention, while the activity of the right was unimpaired.

3. It may give evidence of mitral regurgitation much as the ventricular form of venous pulse gives evidence of tricuspid regurgitation (Minkowski). Many of the curves, however, which were published as characteristic of this condition, showed no deviation that might not be found in perfectly normal tracings (Young and Hewlett). Edens,

also, after a rather extensive experience with optically recorded esophagrams, found no typical type of curve in these conditions.

4. It has been suggested that the method might give evidence of adhesive pericarditis, especially in cases in which the systolic negative apex beat is absent. Edens, however, found no characteristic tracings in this condition.

It is evident that the method only supplements the information given by the jugular tracing in cases in which the interpretation of the latter is in doubt. That the esophageal pulse more nearly approximates the pressure variation in the auricle than the jugular pulse is evident, but its usefulness is limited by the fact that the movements of the heart may, under special circumstances, become its predominant factor. On the whole, it must be stated that the registration of the esophageal pulse has not contributed appreciably to our understanding of the circulation.

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CHAPTER XIV.

THE APEX BEAT AND CARDIOGRAM.

If the finger is placed over that region of the chest corresponding to the apex, an impact is felt that is spoken of as the *apex beat*. Although much discussion has arisen as to its cause, it has always been recognized as representing the beginning of ventricular systole. The graphic record of this impulse is termed a *cardiogram*.

METHODS OF RECORDING.

For reasons of convenience the direct registration of cardiograms by levers has been almost entirely replaced by that of air transmission systems. The simplest procedure consists in applying a round or horizontal box-shaped receiver over the impulse area and transmitting the movements of the skin through tubing to a recording tambour. This method is at once the oldest, simplest and best. As in the transmission sphygmograph, the chief desideratum for accurate work is a recording mechanism having a sufficient vibration frequency. This no tambour recording on a smoked surface or with ink pens can possibly have. Use has, therefore, been made of optical capsules (Frank and Hess, Wiggers, Weber, Weitz) and the interference bands of the micrograph (Crehore).

A more complicated transmission occurs in the use of the cardiograph first devised by Marey and subsequently modified by a number of investigators (Kronecker). The cardiograph of Marey consists of a tambour covered by heavy rubber, in the center of which is a button brought into apposition with the impact area. In some forms, as that by Edgren, a spring is placed inside of the capsule, making this instrument, in contrast to the funnel receiver, not a mere volume recorder but a tension apparatus. A tension recording instrument would be necessary if the recorded curve represented a record of intraventricular pressure. A sane consideration of physical and anatomical facts, however, makes it difficult to conceive how this can be the case, for the intraventricular pressure variations not only fail to be transmitted through the thick apical and thoracic musculature, but the relation of the apex to the chest wall changes during the cardiac cycle. Even if the cardiogram could be shown to possess a contour identical with that of the intraventricular curve—which has not been accomplished—it would not be proof that they represented the same thing. We may assume, with reasonable surety, that the *apex beat represents only the*

varying pressure of the cardiac apex on the thoracic tissue; and this is solely governed by the shifting of the heart's position and its degree of filling. In recording these movements through the skin and intercostal muscles, nothing is gained by a tension recording device of such a construction as the Edgren cardiograph.

Nature of Cardiograms Obtained by Recording Tambours of Adequate Efficiency.—Cardiograms taken with reliable forms of apparatus have not been extensively published. Frank and Hess reported a diagram of what they consider a typical cardiogram in the dog. Records not unlike this have been obtained in man (Fig. 80) (Wiggers, Weber). More than a tentative explanation of such records

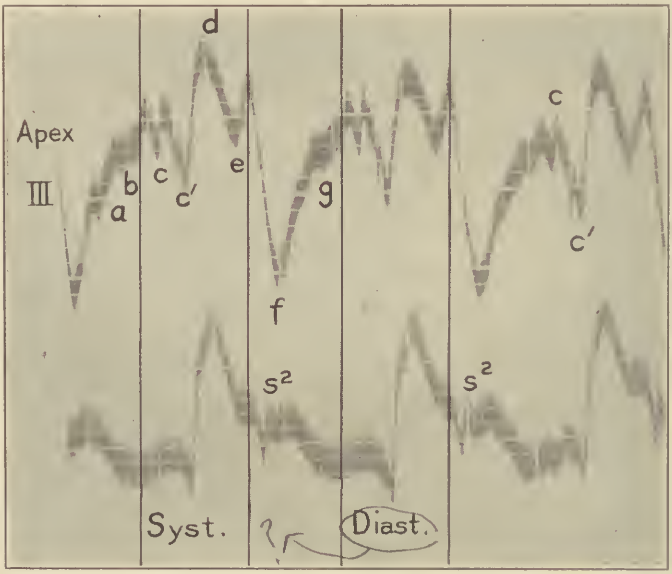

FIG. 80.—Optical tracings of cardiogram and subclavian pulse. *a b*, auricular systole; *c*, initial heart-sound vibrations; *c′*, valve vibrations of first sound; s^2, vibrations of second sound indicated on subclavian pulse (*cf.* with Fig. 102).

is impossible at present. The curves begin with an oscillation, *a–b*, that may conceivably be due to auricular contraction. Ventricular systole is inaugurated by a series of sharp vibrations due to the first sound. There are apparently two groups of these vibrations: *An initial set* of longer period, *c*, and a *final set* of shorter period, *c′*. They last at least through the isometric period. As soon as the ejection period begins, as shown by the subclavian rise, the curve slowly rises to its maximum, *d*, and then slowly recedes again, *e*. This can be explained by assuming that early in ejection the heart continues to move downward and presses more firmly against the chest wall, but during its later phases the apex gradually moves away, owing to the

diminution in ventricular volume. At the beginning of diastole (probably) a rapid drop to f takes place. This can be explained by assuming that the apex moves upward in the beginning of diastole. Finally, however, as the ventricle fills the apex is again pressed against the chest wall more firmly and occasions the slow diastolic rise g.

It is incorrect to designate such a curve as a *typical curve*. The writer is inclined to believe that there is no "typical curve." If the receiving tambour be moved only $1\frac{1}{2}$ cm. to the right the contour of the curve changes. The heart sound vibrations may still be recognized, but the systolic curve is directed downward, indicating that that particular part of the heart moved away during the entire systolic phase (*negative cardiogram*). If the tambour is displaced 1 cm. to the left of its original position the curve becomes entirely positive but of different contour (Fig. 102). After the typical heart sound oscillations, c, the curve rises sharply to a peak, d, and then slowly draws away during the rest of systole (*cf.* also more recent graphs and interpretations of Weitz).

It is evident that slight variations in the position of the receiving tambour modify in pronounced fashion the contour of the cardiogram—probably because the relation of the heart to different points on the chest wall varies greatly.

Similar conclusions have been arrived at by Crehore, who reported the details of cardiograms reconstructed from the micrograph interference bands. His curves also give evidence of preliminary oscillations similar to c–c'. He concluded that the ejection period occurred somewhere within this group of waves rather than after it, as interpreted by the writer.

CLINICAL VALUE OF CARDIOGRAMS.

In estimating the clinical value of cardiograms it is desirable to consider separately those taken with polygraph tambours and those recorded with apparatus of adequate efficiency. The former have been used for the following purposes: (1) To determine the *As*–*Vs* interval: (2) to mark exactly the onset of systole; (3) to determine, by its conformation, the presence of hypertrophy; (4) to distinguish right-sided from left-sided hypertrophy; and (5) to determine whether a pulse deficit is present.

In none of these capacities may the ordinary cardiograms be considered of any value. Optical tracings indicate that the onset of systole is frequently not accompanied by an immediate rise of the curve. If we added the delay in the rise of the tambour lever it is apparent that the onset of systole can be established only approximately in this way. Since this is the case, neither the presphygmic period nor the *As*–*Vs* conduction time can be accurately estimated by comparing other pulses with the apex tracing.

Tracings taken by means of optical apparatus also indicate that curves of exceedingly varied contour may be obtained from perfectly normal subjects; that from the same subject, in fact either positive or negative tracings may be obtained by shifting the tambour slightly.[1] The latter are, therefore, of no diagnostic significance.

Although useful in a didactic way to demonstrate the existence of a pulse deficit, the cardiogram supplies no evidence not obtainable by auscultation for the heart sounds. It may be pointed out, in this connection, that every ventricular systole may not give a typical cardiogram. Due to the varying volume of the ventricles, the varying approximation to the chest wall and the changing force of systole, it is sometimes impossible to determine whether two consecutive waves are associated with the same systole or belong to two rapidly following beats. On the other hand, a feeble systole often gives no record at all.

Optical tracings of the apex beat have so far been shown of value in only one respect, namely, that they incorporate the heart sounds and so allow an exact establishment of systole and diastole. According to Weber, they enable us to determine the beginnings of auricular systole, ventricular systole, systolic ejection and opening of the *A–V* valves, and are further particularly valuable in determining the isometric contraction phase. It is quite obvious, however, that the same temporal relations may be established quite as well by the use of the optical venous and arterial pulses. Whether any other significance may be attached to pathological tracings, further investigation alone can determine. Weitz it is true has published a large series of optically recorded cardiograms both from normal individuals and from those with cardiac lesions. Aside from the addition of a variety of murmur vibrations associated with the particular lesions in question and the greater predominance of positive waves, they show nothing that can be regarded as distinctive, in a diagnostic sense.

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[1] *Cf.* Figs. 64, *A;* 80 and 102.

CHAPTER XV.

THE ELECTROCARDIOGRAM.

APPARATUS, TECHNIC AND CRITIQUE.

THE fact has long been recognized that a state of electrical negativity accompanies the spread of the excitation process through animal tissues. In a previous chapter (*cf.* page 22), the way in which these action currents have been utilized to follow the excitation wave across the heart was analyzed. In this chapter, the principles and practice of recording and interpreting the electrical variations derived from indirect limb leads will be considered more in detail.

The Capillary Electrometer.—To measure the difference of potential or the electromotive force the capillary electrometer was first employed. A description of this instrument is given in all modern text-books of physiology. It has certain advantages, two of which are: That it is relatively inexpensive and lends itself to the detection of minute currents (0.013 millivolt), which it records without a latent period. The excursions are proportional to the electromotive force when the capillary is of even caliber and are not influenced by variations in external resistance. It is, therefore, possible to use this instrument, as was done by Kölliker, Müller, Waller and Bayliss and Starling, to detect the presence of rapidly recurring electrical variations in the hearts of animals and of men. In order to maintain a sufficient degree of sensitiveness, however, the apparatus must be so adjusted that neither the contour nor the size of the rapidly recurring electrical variations is correctly reproduced and the curves obtained demand reconstruction. This can be done after the scheme formulated by Garten. The most practical objection to the use of the capillary electrometer—and the one, no doubt, that has limited its application in clinical work—is the fact that the instrument is so readily disarranged. For this reason it has been almost entirely supplanted by the string galvanometer in recording electrical phenomena.

The String Galvanometer.—The string galvanometer, the development of which in its modern form is almost entirely due to the ingenuity of Einthoven, is based upon the principle *that when a conductor carrying an electric current is placed at right angles to a magnetic field the conductor moves in a direction at right angles to both the field and the current.* Thus, as is shown in Fig. 81, if a current passes down a very light fiber of silvered quartz, *C*, placed in the field of two electromagnets, *S* and *N*, the fiber will move in the direction shown by the arrow *a*. In the best Einthoven galvanometers the string is made of silvered quartz and varies from 2 to 4 μ in diameter, and is consequently visible to the

naked eye only in very intense light. The tension of the string may be increased or decreased by a micrometer adjustment attached to the upper connection. The electromagnets are excited by connecting them with a 10-volt storage battery. The movements of the string may be observed by a microscope (Fig. 81, *A*), fitted through openings in the two magnets, or the shadow of its movements may be projected to the lens of a photokymograph by concentrating the heat-free rays of a quiet arc lamp upon the fiber.

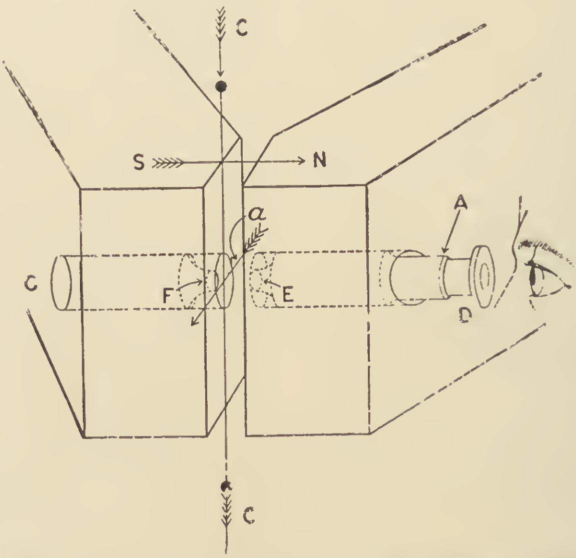

Fig. 81.—Diagram illustrating the principle of the string galvanometer. (After Lewis.)

Galvanometer Models.—Owing to the great expense involved in the construction of the string galvanometer devised by Einthoven as well as technical difficulties encountered in its operation, the original model of Einthoven has never been developed commercially, the only replica of the Einthoven instrument built after constants of the Leyden apparatus being located in Prof. Williams's laboratory at the College of Physicians and Surgeons, New York City. The commercial models in use are those of Edelmann & Sons, Munich, that of the Cambridge and Paul Instrument Co., known as the "Cambridge model," and that designed by Prof. Williams and now manufactured by the Charles Hindle Co. and known as the "American model."[1] The latter forms are

[1] Since the above was written the author's attention has been directed to the Fahr-Stoppani model manufactured by Stoppani, Berne, Switzerland. According to the schematic diagram shown in the catalogue, this construction follows that of the original Einthoven and also the Edelmann types, in the sense that the galvanometer tubes pierce the core of the large electromagnets.

most commonly employed in this country and England. The picture of the "Cambridge model" is shown in Fig. 82. It differs from the construction of the Einthoven and Edelmann models in that the microscopic objectives do not pass through the coil but through the pole shoes of a magnet placed behind them. In this pattern the silvered string is completely enclosed in a "fiber case," shown by the deeper print. As this supplies an air-tight housing, it prevents the slightest disturbance of the fiber due to draughts, excludes the dust which is apt to collect on the fiber and provides a mechanical protection which eliminates the possibility of the fiber being accidentally touched and broken. A milled head is fitted to the fiber case and allows accurate adjustment of the fiber tension. The device for applying the tension is fitted with a safety stop which eliminates all risk of the fiber being broken through overtightening. The fiber case is geometrically sup-

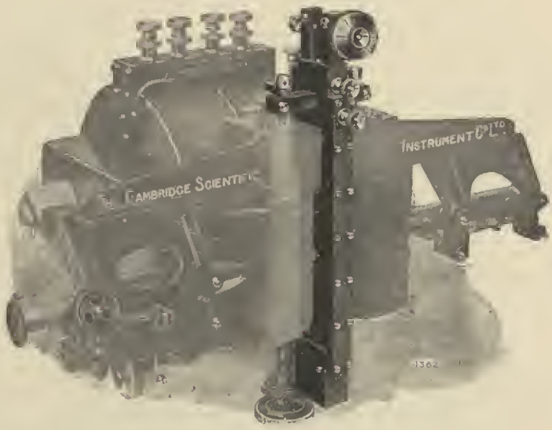

FIG. 82.—Cambridge model of Einthoven's string galvanometer.

ported on the three points and is held in position by a screw and spring. The fiber case can, therefore, be removed after use with the certainty that after replacement the fiber will be returned to exactly the same position in the magnetic field, or, if a spare fiber case is kept on hand, it can be substituted for the other within a very short time. The position of the fiber is arranged, so far as possible, from the influence of the heat developed in the coils, thereby reducing to a minimum the temperature changes occurring in the fiber case, and so giving the apparatus a high degree of constancy. The apparatus is to be commended for its rigid construction and the ease with which it may be adjusted and handled.

The "American model" is shown in Fig. 83. From the physical viewpoint it represents a more perfect type of galvanometer. The illuminating system, being in accordance with the principles out-

lined by Einthoven, permits better definition in the records. In this instrument the magnet is of circular form and consists of a series of helices wound around a central iron core rigidly bolted to the pole shoes through which the microscope tubes pass. This construction not only secures rigidity, but produces field intensities which compare favorably with the original Einthoven apparatus. As the current consumption is small and free radiation of heat is permitted, temperature changes do not affect the string tension and consequently the sensi-

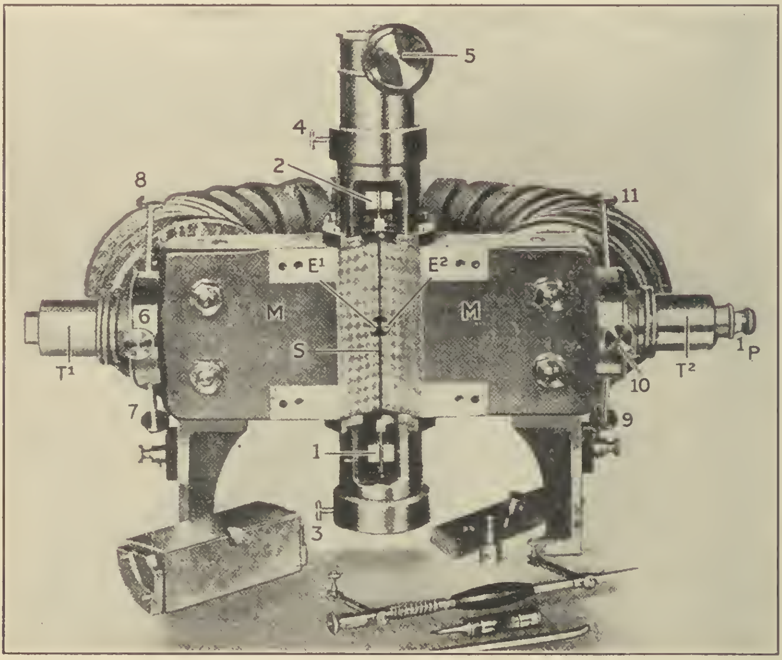

FIG. 83.—"American model" of string galvanometer, opened for insertion of string. *M M*, pole shoes of electromagnet; *S*, string chamber between pole shoes; 1, 2, screws for fastening string; 3, 4, centering screws; 5, adjustment for altering string tension; *T*, T^1, draw-tubes passing through opening in magnets; 9, 10, 11, centering screws; E^1, E^2, objectives; *P*, projection lens. Tools and carrier for transferring strings are shown beside the galvanometer. (After Williams and Hindle.)

tiveness, even when the apparatus is used for long intervals. The string is completely protected against air currents and dust, and no cover is needed over the instrument. Nevertheless, the highest aperture dry lenses can be used. The advantage of this may be appreciated by recalling that an instrument using a 4-mm. apochromatic objective, N. A. 0.95, as this one does, will give the same sharpness of image with three times the magnification, which could be used with an instrument in which a 16-mm. apochromatic objective, 0.3 N. A., is used, or it could be used at the same magnification and would give three times the light.

The large aperture also permits of photographing at much higher rates of speed of the film or paper—up to 5 meters per second. The microscopes are rigidly attached to the magnet, so that the instrument is little affected by external vibrations. Both microscopes have convenient adjustments for centering and each is provided with fine focussing screw adjustments. The adjustments for centering the string in the field are such as to enable the operator to secure the condition that the string can be tightened and slackened over the entire useful range of tension without appreciable change of focus or zero—a matter of considerable importance. The deflections are proportional to the strength of current throughout the string for 6 to 8 cm. either side of zero, with a magnification of 900 diameters, the usual magnification desired. (None of the foreign commercial instruments give better than 3 cm. to either side of zero with the magnification possible.)

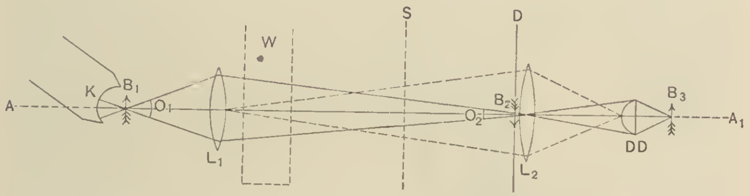

FIG. 84.—Diagram of Einthoven's optical system for string galvanometer. K, positive crater; B_1, luminous point in front of crater; A–A_1, optical axis; L and L_2, lenses; $D\ D$, achromatic microscope objective; B_3, galvanometer string; W, water cooler; S, focal place for positive carbon; B, iris diaphragm. (After Einthoven.)

The Optical Arrangement.—A number of different optical systems have been used in order to project the shadow of the string at right angles to the slot in a photokymograph placed from 1 to 1.5 mm. away. Of these different systems, that employing the principles originally described by Einthoven gives the best definition in records and is one of the illuminating systems furnished with the American model. The principles of this illumination system are indicated in Fig. 84. The crater of the positive carbon, K, the lenses, L_1 and L_2 (10 and 5.5 diopters respectively), the diaphragm, D, and the illuminating objective, $D\ D$ (achromatic objective, N. A. 0.85), are centered in the optical axis, A–A^1. The distance from K to L is so adjusted that a picture of the crater is projected in the plane, S, 63 cm. in front of L_1. This causes the clear projection of the luminous point, B_1, in the plane, B_2, just behind the second lens, L_2. This lens then projects a clear picture of L_1 upon the objective, DD. Finally a sharp projection of B_2 upon the string, B_3, is made by adjusting the focus of the illuminating objective, DD.

The shadow of the illuminated string is projected by a 4-mm. apochromatic objective, N. A. 0.95, through a projection ocular and

focussed upon the slit of a photokymograph placed from 1 to 1.5 meters away.[1] In order to obviate the inconveniences attached to the use of an arc lamp, a number of attempts have been made to supplant it by some form of gas-filled bulb. The most successful of these devices are the "Pointolite" lamp obtainable as the illuminating system with the Cambridge galvanometer and the incandescent Tungsten bulb supplied by the Hindle Company. These illuminating systems have the further advantage that the length of the entire apparatus may be reduced more than a meter. They have the disadvantage that the illumination is decidedly less intense and, con-

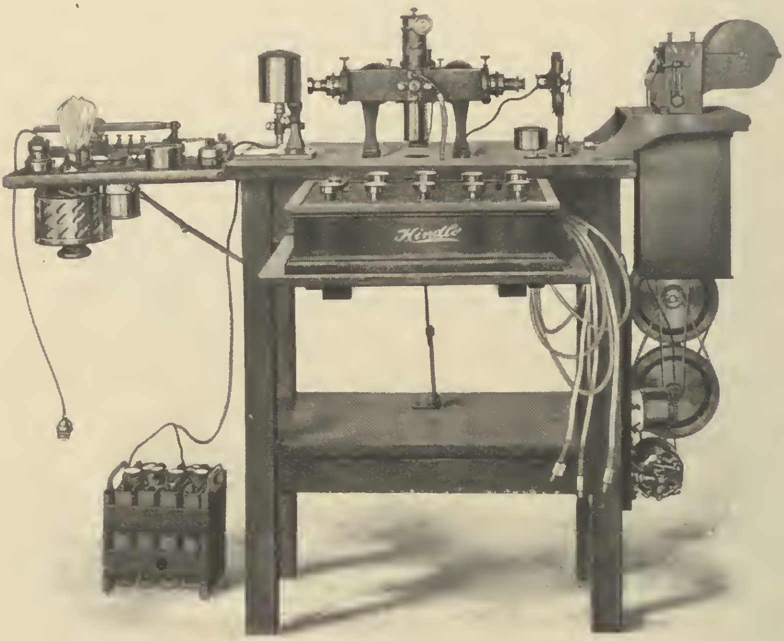

Fig. 85.—Compact model of American electrocardiographic apparatus for office and hospital use, employing bulb light for illuminant. (Courtesy of Mr. Hindle.)

sequently, does not suffice for records taken at rapid speed of film, 25 mm. being about the maximum. The entire electrocardiographic apparatus equipped with this type of illuminating system is shown in Fig. 85.

The Electrodes.—Three electrodes are applied respectively to the two arms and left leg and connected with the galvanometer through a key and resistance box.

[1] For further details, see Einthoven: Arch. f. d. ges. Physiol., 1910, **130**, 287. No one should undertake electrocardiographic work until he has thoroughly digested the principles of electrocardiography as expounded in this classical paper.

Originally some form of nonpolarizable electrode was considered indispensable. These consisted of saline baths contained in large porous receptacles which, in turn, were immersed in a larger bath containing zinc sulphate solution (*cf.* Edelmann catalogue) or of pads soaked in saline and resting upon porous plates separating the saline from the zinc sulphate solution (*cf.* Cambridge and Paul Instrument Company's catalogue). Into the zinc sulphate solution dipped strips or sheets of zinc, which when connected with the galvanometer wires complete the circuit.

Such nonpolarizable electrodes, which require a great deal of attention in order to keep them clean, are now known to be unnecessary except in very special work. Convenient electrodes may be made of deep vessels containing 20 per cent salt solution, into which sheets of

FIG. 86.—Photograph illustrating Williams' electrodes in use. (After James and Williams.)

zinc are directly immersed, or a molded strip of German silver covered with absorbent material bandaged to the arms and leg as shown in Fig. 86.[1]

Time Records.—Time intervals may be recorded in a number of ways. A Jaquet time signal or a tuning fork may be placed immediately in front of the camera slot and, as the entire field is flooded with light, the shadows of pointers attached may be recorded at one margin of the paper. Usually some form of rotating motor, such as shown

[1] For details as to the choice of electrodes and the factors that must be taken into consideration in their selection and application, see Einthoven (Lancet, 1912, **1**, 853), Lewis (Jour. Physiol., 1915 (Proc.), **49**, i), Waller (Jour. Physiol., 1915 (Proc.), **49**, xliii), Pardee (Am. Jour. Physiol., 1917, **44**, 80), Felberbaum (Jour. Lab. and Clin. Med., 1919, **4**, 497), Cohn (Arch. Int. Med., 1920, **26**, 105) and Dresbach (Am. Jour. Physiol., 1923 (Proc. December, 1922, Meeting).

in Fig. 87, is introduced at some focal point so that it interrupts the light momentarily and causes the production of fine vertical lines on the developed film. In the Cambridge and American model this is a synchronous motor actuated by a 50 v. d. tuning fork, on the armature shaft of which is a small disk carrying five spokes, one of which, being wider than the others, records a broader line. The speed of rotation is such that every fine line thus recorded represents 0.04 second and every fifth line 0.2 second (*cf.* Fig. 89). The horizontal lines representing millimeters and centimeters are produced by a large scale etched on the cylindrical camera lens. It is obvious that a perfect cross-section coördinate effect, such as shown in Fig. 89, is obtained when the film moves at a pace which is exactly ~~1 cm.~~ in 0.2 second.

½ cm

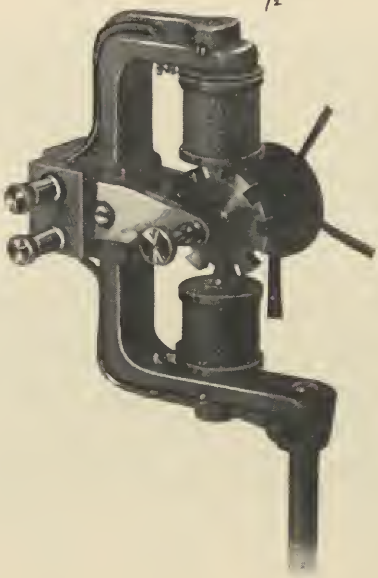

FIG. 87.—Rotating synchronous motor actuated by tuning fork for producing abscissæ time-lines on record. (Courtesy of Mr. Hindle.)

Procedure in Recording Electrocardiograms.—By connecting any two of the electrodes in such a way that the photographed shadow moves up when the base of the heart is negative, it is possible to tap the heart currents in three different places, or, as generally worded, we obtain three different leads, namely:

Lead I.—Right arm, left arm.
Lead II.—Right arm, left leg.
Lead III.—Left arm, left leg.

In order to facilitate the taking of these three leads in rapid sequence, they are not directly connected with the galvanometer circuits, but to

a special switch, schematically shown in Fig. 88. By rotating a knob so that the bars come into the position indicated by *I*, *II* and *III*, corresponding leads can be connected with the galvanometer without changing the wires from the electrodes of the patients. Should any one of these leads be connected with the galvanometer directly, even when the body is entirely relaxed, so great a flow of current would result that the string would be thrown from the field and possibly broken. This great and direct electrical current is due to the activity of the innumerable glands and is called the *body current*. In order to record the alternating current generated by the heart it is, therefore,

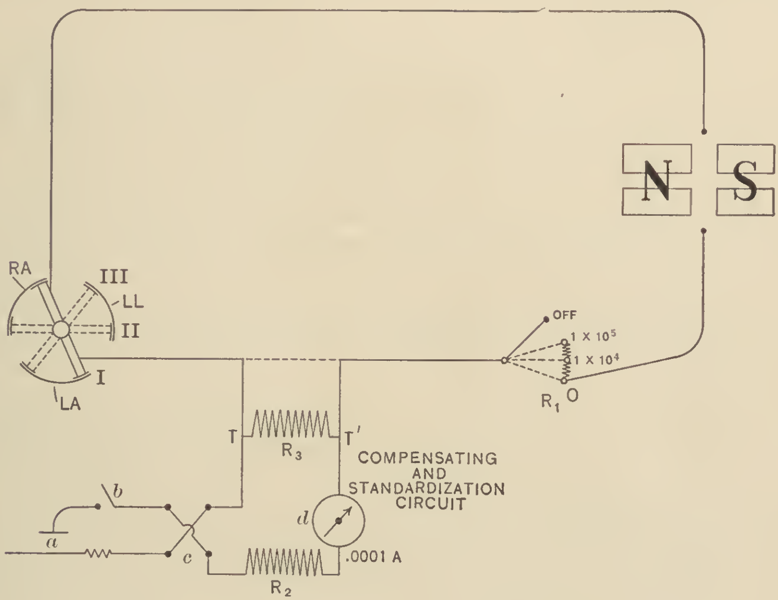

FIG. 88.—Scheme showing connection of patient with galvanometer and also Einthoven's method of compensation and standardization, as adapted to the American model of the string galvanometer. Description in text.

necessary to first *neutralize* or *compensate for* this direct current by introducing a counter-current in an opposite direction. This is accomplished in the following manner: The body is at first not directly connected with the string galvanometer but through a variable resistance (Fig. 88, R_1). At first 100,000 ohms are thus introduced for the protection of the string. When this is done the sensitiveness of the galvanometer is reduced and the body current causes only a very slight deviation of the strings to the right or left. This is now neutralized as nearly as possible by introducing an equal voltage in the opposite direction through a *compensating circuit*. In this circuit,

as shown in Fig. 88, the current from a dry cell (about 1.5 volts) passes through a switch, *b*, a pole changer, *c*, and then through a variable resistance, R_2, sufficient to pass a current of 0.0001 ampere through a microammeter, *d*. In parallel with this circuit is placed a variable resistance, R_3, which is so adjusted that for every ohm of resistance introduced there will be a difference of potential of 0.1 millivolt across the terminals, $T-T^1$. After the body current has been neutralized as nearly as possible by introducing the requisite number of ohms' resistance in R_3, the resistance at R_1 is decreased to 10,000 ohms and finer compensation of the body current made again. Finally, all resistance is thrown out of circuit at R_1 and the body is thus directly connected with the galvanometer.

The string is next *standardized, i. e.*, its tension so adjusted that 1 millivolt of current causes a deflection of the string shadow in diastole equal to 1 cm. This is tested by introducing 10 ohms' additional resistance in R_3 and noting the string deflection. If this is less than 1 cm. the string is loosened; if more it is tightened.

After these steps have been carried out the electrocardiogram is recorded, but it must be emphasized that these procedures should be repeated in taking of each lead. All of these procedures, that is, *standardization, compensation for body currents*, as well as estimating the external resistance, are accomplished by convenient electrical devices, the details of which may be obtained from the catalogues of manufacturers.

Summary of Steps in Taking Electrocardiograms with the American Model.[1]

1. Make certain that all compensating resistances are at zero and that the galvanometer switch is off.

2. Apply electrodes to subject, taking care to connect with appropriate wires.

3. Close arc-light circuit and focus crater on a diaphragm thrown temporarily into position at a distance of 63 cm.

4. Close magnet circuit from storage cells. (The string should not move out of focus if properly centered.)

5. Connect Lead I by switch.

6. Turn reversing switch to *A* and have microammeter read "10."

7. Test direction of body current by turning protecting resistance to 10^5; note direction of shadow deflection.

8. Introduce current, 1 millivolt at a time. If string moves farther away from center change reversing switch to *B* and again introduce counter-current until the string shadow is back to zero.

9. Turn knob, introducing protecting resistance to 10^4 and introduce sufficient counter-current to exactly neutralize body current.

[1] For technical details as to operation of "Cambridge model," *cf.* Lewis, Mechanism of Heart Beat, 1920, p. 32 et seq.

10. Turn string circuit on without resistance.
11. Standardize string, note position at rest, then introduce 1 millivolt into circuit. Tighten or loosen string until deflection equals exactly 1 cm.
12. Start tuning fork and synchronous motor.
13. Adjust light again, if necessary, bring back diaphragm and string to a clear focus.
14. Record a strip of record.
15. *Turn off string first* and then bring all resistances back to "zero."

Repeat, beginning with step 5 for Leads II and III.

After Completing All Three Leads.

1. Turn off string and bring all resistance to zero.
2. Turn reversing switch to zero.
3. Turn off magnet circuit, watching string shadow.
4. Stop tuning fork and motor.
5. Turn off arc light.

(In order to avoid technical blunders leading to the breaking of strings the author requires all novices to follow the foregoing procedure strictly.)

Testing of the Galvanometer.—It is important to remember that the deflection for any given string is proportional to the amperage and not to the voltage. It varies also with the length, diameter, composition, preparation and tension of the string. To utilize the apparatus as a voltmeter the standardization before explained is necessary. In order to accomplish this with a variable external resistance, either the resistance of the string must be altered or its tension changed. The latter is the more convenient procedure and the one generally employed. It is obvious, furthermore, that the relation between the actual deflection of the string and its shadow on the photokymograph depends on the optical magnification (that is, the lens magnification and the distance from the photokymograph). It is quite evident that those investigators who, on account of inadequate illumination or inferior lenses, are forced to work with a magnification of 100 to 200 require a much greater actual deflection, and hence must employ a string under less tension than those who are able to utilize a magnification of 600 to 1000. Unfortunately, however, as the string is slackened, the deflection time, which is the time interval between the zero position and the final level, is increased. This is well shown in the following table compiled from the results of Samojloff:

Sensitiveness.	Magnification.	Deflection time.
1 millivolt = 1 cm.	800	0.024 second
1 millivolt = 1 cm.	400	0.060 second
1 millivolt = 2 cm.	400	0.100 second

This leads to the discussion of the qualifications of a reliable instrument and the methods by which they may be determined. As Einthoven has pointed out, a perfect galvanometer has not yet been constructed, but the error can be reduced to a point where it is negligible. Fahr, who has recently made a theoretical analysis of the string galvanometer, has shown that the string must have an inherent vibration rate at least five times as great as the rate of vibration to be recorded if the error is to be reduced to 4 per cent; whereas it is necessary that the inherent rate of the string should exceed the vibration ten times if the error is to fall to 2 per cent. Fahr very practically points out that since the tension of the average string 10 cm. long cannot be safely increased, so as to give more than 1000 vibrations per second, the electrical variations recorded should not exceed 200 per second.

Given an instrument with a vibration rate five times as great as the vibration to be recorded, we may be certain that it is reliable for practical purposes, provided the combined air and electromagnetic damping is sufficient to render the string aperiodic.

There is, however, another and more practical way in which the efficiency of an instrument may be tested, namely, by determining experimentally the longest deflection period permissible without causing any alteration in the height and contour of the curves. Samojloff, Einthoven and Lewis have made such determinations. The curves of Lewis show that when the deflection time becomes greater than 0.02 second a distortion of the electrocardiogram waves occurs. Briefly stated, the amplitude of the *R* wave is too small and that of the *T* wave is relatively too large. An evident failure on the part of some clinicians to comply with this requirement discounts seriously any significance they have attributed to slight variations in the height of these waves. *If it can be shown by supplementary tests that the string is aperiodic and the deflection time is* 0.02 *second or less it may be inferred that the instrument is sufficiently accurate for all practical purposes.*

Simultaneous Registration of Other Phenomena.—It is frequently desirable or necessary in clinical practice to record other dynamic events synchronously with electrocardiograms. In the case of polygraphic records the tambour levers may be placed directly in front of the camera slot or in the American model, having the Einthoven system of illumination also just before the condensing lens, L_2, Fig. 84. Optical records of arterial and venous pulses, as well as *heart sounds*, may be simultaneously recorded by placing the optical capsules and lamp arrangement, illustrated in Fig. 61, on a table extension in front of the galvanometer. In such multiple registration one-half of the field may be used for the electrocardiogram and the other for the mechanical records. The side used for the latter may be screened from the galvanometer light by placing an opaque sheet in front of lens, L_2; but this is unnecessary, as the intensity of the light reflected from the mirror

is greater than that of the galvanometer. Such synchronous records of heart sounds and electrical variations are shown in Fig. 166.

For research purposes,[1] largely, it is sometimes necessary to record two or more electrograms or electrocardiograms simultaneously. This involves special technic which is far from simple. In general, three methods have been employed, viz.:

A. Two galvanometers arranged side by side at a slight angle, and illuminated by their own optical systems, project two separate fields upon the camera slot. By attention to alignment, equal illuminating intensity, equal standardization and the prevention of overlapping by means of a screen, satisfactory records may be obtained.

B. Two strings are mounted in the same housing, as in the Cambridge apparatus, and their shadows directed by prisms into the same camera slot.

C. The alignment of two galvanometers in the same optical axis. (For more detailed review of different methods and detailed technic required, *cf.* Einthoven, Bergansius and Bijtel.)[2]

THE NATURE OF THE RECORDS AND THEIR INTERPRETATION.

Terminology.—The normal *electrocardiograms*, as the records are termed, are characterized by three or four positive variations, and generally by two sharp negative waves (Fig. 89). Different terminologies have been used to designate these waves. Bayliss and Starling, who first recorded a triphasic current with the capillary electrometer, call the second and third variations the *initial and terminal phases* of the ventricular current. They also applied the term *spike* to the large, sharp wave. Realizing that the electrocardiogram could be open to different interpretations, Einthoven, in 1895, introduced the alphabetical designation P, Q, R, S, T and more recently U, a terminology that has been almost universally followed. To indicate the lead in which the wave occurred the Roman suffix is usually added in descriptions. Thus, R_{II} means the R wave obtained by Lead II, etc. Kraus and Nicolai, partly because they believe the letters should in some way indicate the cause of the waves and partly because they think that the letters used by Einthoven have been used in pathological cases to designate waves of diverse origin, suggest a nomenclature of their own, namely, A $(=P)$, the atrial wave; J $(=R)$, the initial ventricular wave; and F $(=T)$, the final variation. The interval between A and J is indicated by h, since this is considered the time that elapses in passing the His bundle. The nomenclature of these authors

[1] For certain experimental purposes it has also been found desirable to amplify the excursions of the galvanometer string through the use of thermionic vacuum tubes For details the following articles may be consulted: Forbes and Thacher: Am. Jour. Physiol., 1920, **52**, 409; Gasser and Newcomer, Am. Jour. Physiol., 1921, **57**, 1; Daly and Shellshear: Jour. Physiol., 1920, **54**, 287.

[2] *Cf.* also Cohn, Heart, 1923, **9**, 314.

has, however, been received with little favor and seems entirely unnecessary for the reasons given by them.

Time comparisons have shown that of these variations the P wave alone is associated with auricular activity while the other waves are related to ventricular systole. Consequently, we speak of *auricular* and *ventricular complexes.* The auricular complex rises slowly to a summit, P, which is either rounded or peaked and is followed by a

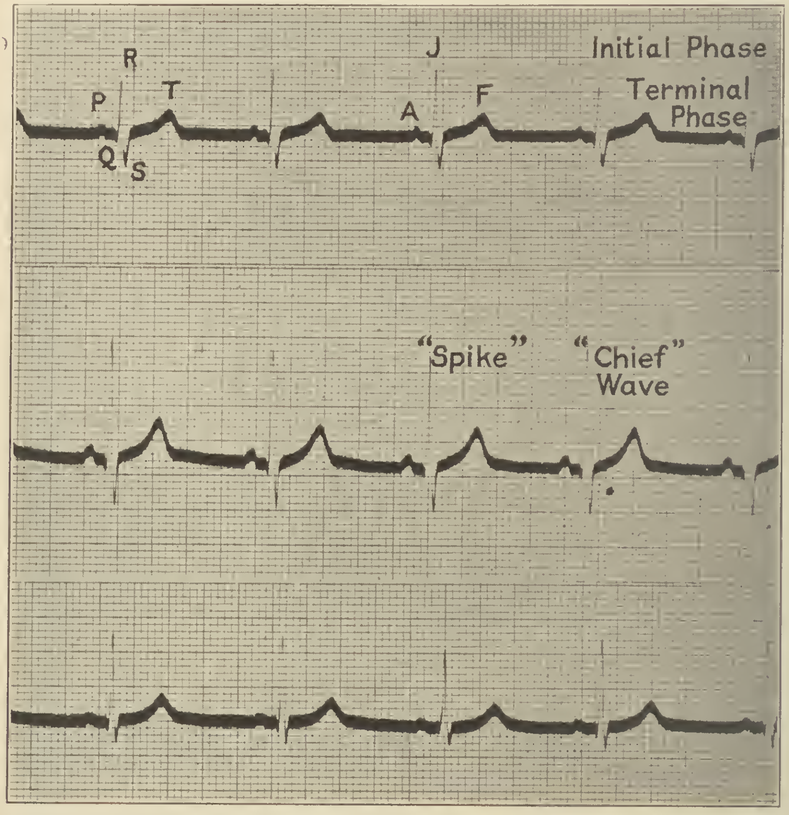

FIG. 89.—Normal electrocardiograms of a healthy young man—three leads; abscissæ 1 div. = 0.04 second; ordinates 1 div. = 10^{-4} volt. The terminologies suggested by various investigators are indicated. (Courtesy of Dr. H. B. Williams.)

drop to a base line or isoelectric potential. The ventricular complex may begin with a small depression, Q, or this may be absent in all leads. The steep spike R, which either returns to the base line or passes below, forming a variable dip, S, is constantly present, however. This entire complex, which takes less than 0.1 second, is referred to as the *initial deflection,* while the smaller T wave toward the end is spoken of as the final or *end deflection.*

Time Relations.—As a result of careful experimental work, the relation of the separate deflections both to the spread of negativity throughout the heart and to dynamic events of the cardiac cycle have been established (*cf.* Fig. 90). For this purpose Lead II has usually been chosen, largely because the waves are generally larger and more certain in the direction of deflection.

Relation to Spread of Excitation Wave in Heart.—The following relations of the waves of the electrocardiogram to the point of excitation seem to have been established: The rise of P_{II} begins approximately 0.01 second after initial negativity of the *S–A* node; about 0.03 second later, or midway on the ascending limb of the *P* wave, the right auricular appendage has been excited, while within 0.045 second, or approximately at the summit of P_{II}, the ear of the left auricle becomes electrically negative (Eyster and Meek, Lewis, Meakins and White, Wedd and Stroud).

The earliest evidence of negativity in the ventricle, according to Lewis and Rothschild, occurs 0.01 to 0.015 second before the upstroke of R_{II}, or about 0.005 second before the Q_{II} depression when present. The "central region" of the right ventricle is negative almost simultaneous with the onset of R_{II}. According to Erfmann, the entire ventricular surface then becomes negative within a few thousandths of a second, but the more detailed investigations of Lewis and Rothschild show that at least 0.02 to 0.03 second is required before the negative wave has spread over the entire ventricular surface. This point coincides approximately with the summit of R_{II} (for literature, *cf.* Wiggers).

Relation to Dynamic and Mechanical Events of the Heart Cycle (Figs. 90 and 91).—Comparison of the P_{II} wave with intra-auricular pressure curves indicates that auricular systole begins near the *S–A* node about 0.02 second after the rise of P_{II} (Garten and Weber, Wiggers), *i. e.*, on its ascending limb. Not until 0.04 second later, however, or until the entire *P* wave has been completed, has the tissue near the right auricular appendage even begun to contract. About 0.075 second after the rise of P_{II} the dynamic phase of auricular systole is over, but auricular systole, as commonly defined, does not end until 0.125 second after the rise of P_{II}.

The relation that the termination of auricular systole bears to the R_{II} variation is determined largely by the *P–R* interval; in a certain measure also by a slight variation in the length of auricular systole. Taking the interval 0.105 as an average duration of auricular systole and adding 0.02 for delay of contraction after excitation, it is evident that if the *P–R* interval equals 0.125 second, the end of auricular systole coincides with the beginning of R_{II}. If the *P–R* interval is shorter than 0.125 second, or if the duration of auricular systole is larger by only a few hundredths of a second (both very common in the dog), then auricular systole extends into the time interval occupied by the *R* variation (Fig. 91). This means that in such cases the entire auricle

still continues to shorten after the excitation wave has spread to the ventricle. On the other hand, if the P–R interval in Lead II is longer than 0.125 second (which is common in man) then auricular systole

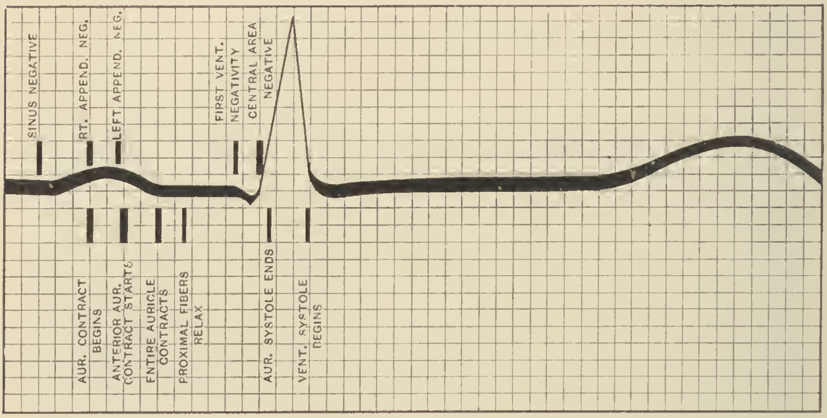

FIG. 90.—Diagram showing waves of electrocardiogram, Lead II, and their time relations, *a*, to primary negativity of a few regions of heart and *b*, to mechanical changes in auricles and ventricles when P–R interval equals 0.12 second. Abscissæ, 1 div. = 0.01 second.

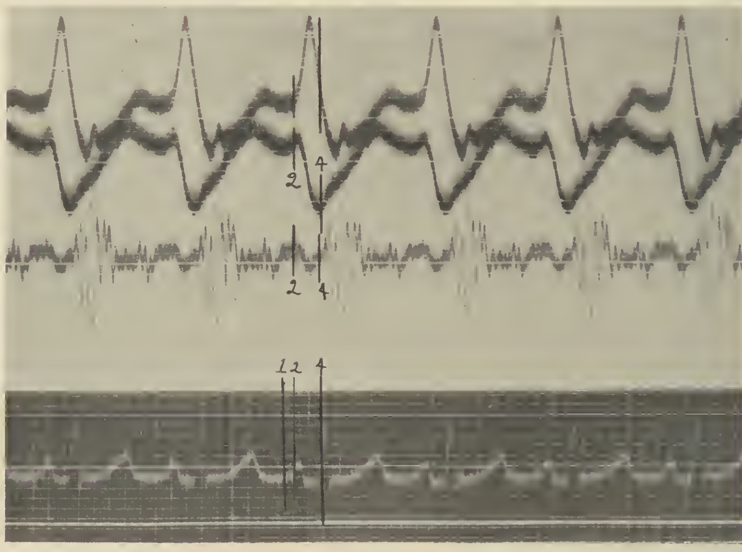

FIG. 91.—Synchronous records of right auricular pressure, auricular myogram, heart sounds and electrocardiogram, Lead II showing time relations of latter to auricular and ventricular dynamic events. 2, beginning of auricular systole; 4, end of auricular systole.

ends before the R variation by an interval equal to the additional lengthening of this interval (Wiggers, Lewis, Feil and Stroud).

As regards the relation of the R wave to the onset of ventricular systole, most of the earlier experimental evidence favors the idea that the R_{II} variation is practically completed before mechanical systole has begun. Kahn registered the movements of a light needle inserted into the right ventricle synchronously with the electrocardiogram. Ventricular systole so indicated began 0.031 to 0.035 second after the rise in R_{II}. A similar delay was shown in the myocardiographic records obtained by Lewis. Previously, Kahn had found that the intraventricular pressure began to rise 0.065 second after R_{II}. It must be concluded, however, that the mechanical apparatus employed by these investigators did not measure up to present-day standards, hence the possibility remains that the delay is not inherent in the heart but is of instrumental origin. Piper was the first to make comparisons with optically recorded pressure curves, but as the electrogram recorded was led directly from the heart and had a configuration entirely foreign to a normal electrocardiogram, his results were of little apparent value. The question was reinvestigated by Garten, who used his electrically recording manometer. He found that the intraventricular pressure began to rise 0.17 to 0.21 second after the beginning of R_{II}, that is, on the ascending limb. This point, it will be recalled, approximately coincides with the end of auricular systole in the dog. In reinvestigating this question by the use of an optical cardiac manometer the author found that the onset of the pressure rise is uniformly somewhat later, that is, 0.03 to 0.045 second after the initial rise of the R_{II} wave. It is significant, therefore, that the R_{II} wave precedes by a short though definite interval the first evidence of mechanical activity in the ventricle

The impression gained by relating the electrical curves to the ventricular myogram is that the T variation occurs during the ejection period of the heart, and that a state of isopotential is reëstablished before the onset of ventricular diastole. On account of the involved nature and, as yet, uncertain interpretation of any myographic tracings from the ventricles, it is difficult to adjudge the value of such observations. Garten determined the relation of the T_{II} variation to the sudden fall of pressure within the ventricle and found that a far greater variation exists than in other time relations. Systole, as a rule, terminated 0.034 to 0.048 second after the T_{II} variation; at other times it terminates as much as 0.11 second before the end of T. The end of ventricular systole is not always marked sharply, however, on the intraventricular pressure curves. In general the sudden fall of intra-aortic pressure, designated as the *incisura* by Frank, offers the most exact indication of the termination of ventricular systole. Garten, and Wiggers and Dean have established the relation of this event to the T wave. These comparisons agree with the results of Garten, in showing

the variable relation of the end of systole to the T wave. *It is quite evident that the end of ventricular systole cannot be definitely related to any phase of the T_{II} variations.*

Relation to the Heart Sounds.—By comparing the recorded heart sounds with the variations of the synchronously recorded electrocardiogram, these relations of the onset and termination of ventricular systole have been confirmed in animals and extended to man. Kahn and Bull, using Weiss's phonoscope, concluded that the first sound vibrations begin 0.03 *to* 0.04 second after the rise of R_{II}, that is, toward its end. These early attempts to establish electrical and dynamic relations are robbed of much of their significance by the fact that it yet remains to be demonstrated that true sound vibrations can be recorded by this apparatus. The comparison of the sound waves recorded by the phonocardiographic method of Einthoven has given similar results in the hands of Lewis, Fahr, and Battaerd, thus confirming the experimental work which places the beginning of ventricular systole on the descending limb of R_{II}. Similar results were also obtained by Dean and the author, who compared sounds directly recorded from the ventricle with Lead II (Fig. 91).

Applying these results to the combined records of the sounds and electrocardiogram in animals and man, we must conclude that *ventricular systole begins about* 0.03 *to* 0.04 *second after the rise of R_{II}, that is, on its descending limb, while the end of systole, as indicated in experimental work, bears a variable relation to T_{II}, but usually follows the event* (Fig. 91).

THE SIGNIFICANCE OF THE ELECTROCARDIOGRAM DEFLECTIONS.

Elementary Principles in Interpreting Records.—Direct Leads.—If the ends of a denervated muscle strip, *A B* (Fig. 92, *I*), are connected through nonpolarizable electrodes with a galvanometer and the muscle is excited at *A*, a diphasic action current is set up in the galvanometer. This is due to the fact that at the moment of excitation the active cross-section, *A*, becomes electrically negative to the resting cross-sections near *B*. By proper connections the galvanometer can be so arranged that this gives an initial upward deflection. As soon as the state of activity reaches *B*, *A* and *B* are equally negative and the deflection reaches its peak. When, a short time later, activity begins to pass off at *A* the deflection descends, and when this portion becomes quiescent and positive with respect to *B* the current flows in opposite direction through the galvanometer and causes a negative or downward dip. Finally, when negativity has passed off entirely the curve returns to an isoelectric base line (Fig. 92, *II*, *A*).

If the same galvanometer connections are used and the muscle is stimulated at *B* a diphasic variation is again recorded; only this time

the initial deflection is negative and the final deflection positive (Fig. 92, *II*, *B*). It is obvious, therefore, that when the nature of the galvanometer connections are known it is possible, from the direction of the deflection, to determine the direction of potential differences and, consequently, the spread of the excitation within the muscle.

When a pair of electrodes are similarly applied directly to the heart—one to the base and the other to the apex—a triphasic variation known as the *electrogram* is recorded. If the connections are so arranged that the electrode corresponding to *A* is applied to the base and that corresponding to *B* to the apex, then it may be supposed that every upward movement indicates predominant negativity or activity toward the base, while every downward movement indicates predominant activity toward the apex.

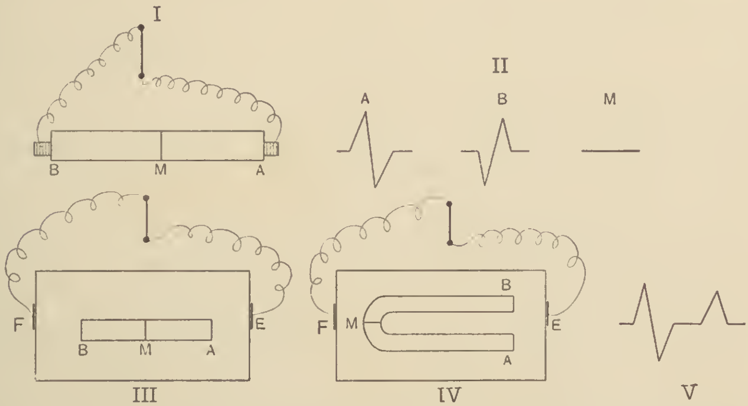

FIG. 92.—Series of diagrams illustrating elementary principles of electrocardiography. *I*, direct leads from end of a muscle strip; *II*, electrical deflections obtainable from same; *A*, when excitation begins at *A*, *B*, when it begins at *B* and *M*, when it starts in the middle; *III*, indirect leads from end of a muscle strip immersed in saline solution; *IV*, similar leads from a U-shaped strip; *V*, triphasic current derived from same when excitation arises at *A*. Further description in text.

Indirect Leads.—In taking electrocardiograms the electrodes are not thus directly applied to the heart, but the currents are led off by way of the conducting tissues of the body. To distinguish such leads from those directly taken from the heart, Einthoven suggested that they be called *electrocardiograms*. If, as shown in Fig. 92, *III*, a strip of muscle is immersed in a bath of saline and we lead off from the ends of the vessel the same sort of records are obtained as when the currents are directly led off from *A* or *B*. The outer walls of the right and left ventricles are more nearly comparable to the limbs of a muscle strip bent at *M* into a U-shape, as shown in Fig. 92, *IV*. If such a U-shaped muscle is stimulated at *M* we obtain a potential difference so that *F* is first negative as regards *E* and later positive as regards *E*. *Vice*

versa, if both A and B are stimulated simultaneously the electrical variations are precisely the reverse.

If, however, A alone is stimulated the side E becomes negative with respect to F until M becomes active and, as activity recedes at A, F becomes less negative to E. As the excitation wave later spreads to B and recedes at M, E again becomes negative as regards F and finally, as negativity subsequently recedes toward B, the curve returns to normal potential. In this way a triphasic curve is produced, as shown in Fig. 92, V. Earlier investigations (notably those of Waller) indicated that the heart lies within the conducting tissues of the chest at such an angle that variations of potential at the cardiac base(*e. g.*, A, B) are led off from the right shoulder or arm, while variations at the apex corresponding to M are similarly spread to the left shoulder or arm and also to the lower extremities. Consequently the idea gained ground that by connecting either, as in Lead I or II, we obtain a fair idea of the relative variations of potential between the base and apex of the heart, *i. e.*, deflections are determined by the so-called *distributed potential differences* (Lewis).

The Earlier Interpretations of Electrocardiogram Deflections.—The idea that electrocardiograms correspond to electrograms seemed to be further substantiated by the great similarity in the recorded waves. Consequently, any explanation pertaining to the waves of one was quite naturally regarded as applying with equal force to both. Experimental studies soon left no doubt as to the fact that the P variation is concerned with the spread of activity across the auricles. Considerable discussion arose, however, as to the significance of the initial Q R S and the final T deflections associated with ventricular activity. Studies of electrograms indicated that a positive deflection, such as R and T, are associated with basal activity, while negative deflections, such as Q and S, are similarly associated with apical activity. According to the working conception of "distributed potentials" then in force, it became the absorbing problem to explain the changing potential variations between the base and apex.

The fundamental ideas of Einthoven at once gained wide acceptance. His interpretation started with the premises that in studying electrical variations of potential we may not regard the base and apex as anatomical divisions. Since the left ventricle largely enters into the formation of the apex, predominant apical negativity was believed to be associated with activity of the left ventricle while predominant activity of the right ventricle was referred to basal leads. In other words, the line of isopotential was supposed to cut the heart, not as in line y–y, but somewhat as in line x–x (Fig. 93, B). Einthoven's interpretation of the separate deflections, stated in terms of present-day knowledge, is also schematically indicated in this figure, and was as follows: Passage of the contraction wave over the A–V bundle and branches produces little variation in electrical potential and is conse-

quently not recorded in the electrocardiogram, but occurs during the isoelectric line, *h*, between *P* and *R*. As the right ventricle, which forms the basal portion of the heart, begins to contract slightly in advance of the left, this accounts for the primary basal negativity and the upstroke of *R* (*cf.* ← 1, Fig. 93, *B*). As the muscular left ventricle then contracts and overpowers that of the right as regards electrical negativity, the apex becomes predominantly negative and the fall of the *R* and *S* waves results (*cf.* 2 in diagram). Equal contraction in both ventricles next leads to a state of equal negativity at both base and apex (*cf.* 3), and this causes the electrocardiogram to return to and remain at an isoelectric potential. Finally, a longer persistence of contraction in the right heart was held to account for greater basal negativity (*cf.* 4) and the *T* wave.

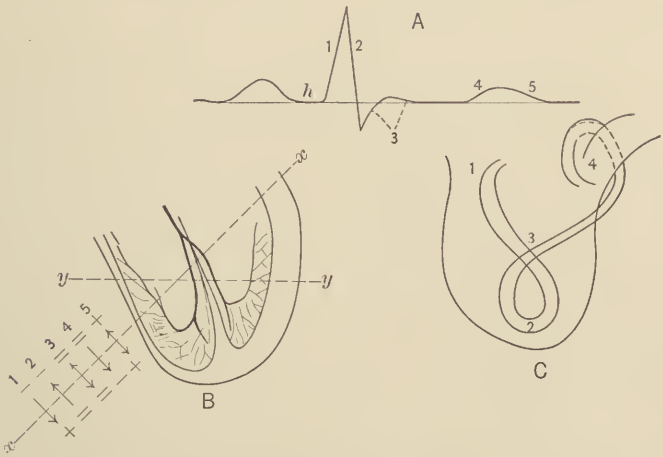

FIG. 93.—*A*, deflections of a normal electrocardiogram; *B*, diagram illustrating Einthoven's interpretation of these waves; *C*, diagram illustrating Gotch's interpretation.

This interpretation, which did not go beyond the facts available at the time, stands in marked contrast to the many attempts to offer more detailed interpretations. Many efforts were made, notably by Kraus and Nicolai, Eppinger and Rothberger, as well as Gotch, to explain the deflection in accord with the excitation of specific layers or bands of muscle. While these interpretations are now largely of historical interest, it may not be amiss to point out by a single illustration how easy it is to fit a plausible and convenient explanation to the facts. We may suppose with Gotch that the contraction wave follows the muscular scrolls of the ventricle, going from the *A–V* ostia to the apex, turning about and returning to the base, ending around the large vessels. As indicated in Fig. 93, *C*, it is then readily explainable how predominant negativity at 1, 2, 3 and 4 could consecutively

give rise to corresponding numbers of electrocardiogram variations. Unfortunately, however, the ventricular contraction does not follow these bands nor has a prolonged activity over the aorta been demonstrated by accurate methods (Eyster and Meek, Lewis).

The earlier investigators interpreted all electrical variations as due to contraction phenomena. A. Hoffmann, probably for the first time, introduced and defended the conception that, with the exception of the final T wave, all deflections are due to action currents accompanying *impulse conduction* rather than muscle contractions. He cited fundamental experiments to show that rapid electrical deflections, such as are represented by *Q R S*, cannot occur in association with slowly contracting muscle, and pointed to the fact that the amplitude of *R* bears no relation to vigor of muscular contraction and that both *R* and *T* may vary independently. He further cited many other observations in man and in animals in support of his views. According to his conceptions, the *spread of the impulses across the auricle* is responsible for the *P* wave, auricular contraction occurring at the same time that impulses are conducted to the ventricle by the His-Tawara system, *i. e.*, during the isoelectric phase following from the end of *P* to *R*. The excitation of the apical layers is responsible for *Q;* its travel in the endocardial arborization toward the base (especially in the right ventricle) causes the *R* rise, after which a return of the excitation to the more apical portion of the left ventricle causes the *S* depression. Not until this time does contraction of the ventricles begin, and it is unaccompanied by any electrical variation except toward the close of contraction, when the *T* variation becomes manifest. This conception of the electrocardiogram as a curve of excitation or impulse conduction plus the end effects of a contraction process is now quite generally accepted as interpreting the essential nature of the deflections. Direct comparisons with the spread of electrical excitation over the heart as well as relative time relations to dynamic events, as previously pointed out, leave no doubt of this general interpretation.

Modern Interpretations.—While such interpretations were gradually crystallizing it became more generally evident to investigators that, after all, electrocardiograms do not represent such simple derivations as base-apex leads from the heart. On the contrary, electrocardiograms obtained from the surface leads of the body are to be regarded as only tapping the resultant currents which, in turn, are made up of many potential differences in various portions of the heart. Taking the action currents developed *at any moment*, we may say that, as a resultant of many variations in potential, there is formed first an *actual potential difference* in the heart at that moment which has a definite direction and magnitude. The direction of this actual potential difference does not lie in a plane which is parallel to the frontal surface of the body, however, and, consequently, only its frontal projection or *manifest value* can be led off from the frontal surfaces or

calculated indirectly from ordinary electrocardiogram leads. By determining the magnitude and direction of the manifest potential differences (*i. e.*, the axis, which the resultant electrical variation takes as projected on the frontal surfaces of the body), we can draw some inference as to the directional spread of the excitation wave at the moment. The principles and practice of determining these values are considered in detail somewhat later (*cf.* page 281).

If the electrical angle and manifest values are determined from instant to instant throughout the cardiac cycle, and these are plotted either as a curve or diagram of arrows, the variation which the resultant potential differences undergo in consecutive deflections of the electrocardiogram can be determined.[1] If, furthermore, these are considered in relation to the architecture of the conducting pathway and the approximate rates of conduction in the His-Tawara system and ordinary muscle fibers, certain inferences may also be drawn as to the significance of these waves. Doing this, Fahr and Weber, and later Fahr, concluded that the excitation process, beginning first in the subendocardial layers of the Purkinje system in the neighborhood of the right papillary muscles, causes the *Q* wave. The excitation process is quickly conducted to the basal arborization of the Purkinje system, however, giving rise to the anacrotic limb of the *R*. While the excitation process is being propagated through the basal Purkinje system, the process in the apical area of the Purkinje system is spreading to the ordinary muscle fibers of the apex. By the time the peak of the *R* is reached the negativity in the ordinary muscle fibers of the apex is of sufficient magnitude to neutralize the preponderance in the basal Purkinje arborizations and causes the catacrotic limb of the *R* and *S* depression. The process meanwhile is passing from the basal Purkinje system into the ordinary muscle fibers of the base. Their negativity increases until the effect of the apical fibers is counteracted and the *S* wave is produced.

The difficulty with this method is that the normal electrocardiogram represents an algebraic picture of the opposing potential variations occurring in the right and left ventricles. To overcome this difficulty, Lewis analyzed the directional spread of the excitation wave from moment to moment, separately in each ventricle. This was accomplished by temporarily blocking the branches to one or the other ventricle and utilizing the earliest portions of the deflections so obtained as curves from the side of the heart with its bundle intact. Thus, when the left bundle is blocked the earliest phases of the recorded electrocardiogram may be taken to represent a dextrocardiogram. Later, he also plotted similar results from cases of probable left and right bundle-branch block in man. Such studies showed that in man the dextrocardiogram usually begins with a small upward deflection *R* in Lead I and a small downward deflection in Lead III. The

[1] For details, *cf.* Lewis: Mechanism and Graphic Registration of the Heart Beat, p. 102.

main deflection, however, is downward in Leads I and II but upward in Lead III. In the levocardiogram the *main deflection* is upward in Leads I and II, but downward in Lead III.

The method of applying such results is illustrated in Fig. 94. Having determined, by the method described on page 281, the direction of the electrical axes at fairly short intervals of time, these may be plotted as a series of arrows (Fig. 94, *A* and *B*). It is evident that in the case of the dextrocardiogram (Fig. 94, *A*) the electrical axis rotates clockwise during the initial phases, being first directed down-

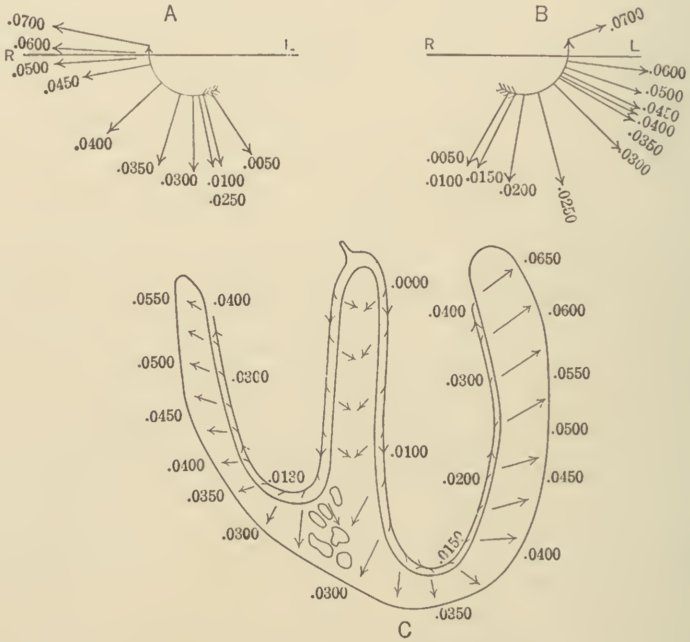

FIG. 94.—*A*, diagram showing rotation of electrical axis during initial phases of the dextrocardiogram; *B*, diagram showing rotation of electrical axis of the levocardiogram; *C*, reconstructed diagram of human heart in section, showing direction of spread through ventricular muscle. (After Lewis.)

ward and to the left (0.005 second) and then in succession downward (0.03 second) to the right (0.04 to 0.05 second) and, finally, upward and to the right (0.05 to 0.07 second). In the levocardiogram (Fig. 94, *B*) the electrical axis rotates counterclockwise, being first directed downward and to the right (0.005 second), then successively downward (0.02 second), downward and to the left (0.03 second), horizontally to the left (0.05 second) and, finally, upward and to the left (0.07 second). Fitting these directional axes in with what we know of the architecture of the conducting system, it is obvious that the scheme of activation shown in Fig. 49, *C*, at once becomes very

probable. As this further accords reasonably well with the relative activation of the ventricular surfaces, as determined by actual experiment (Fig. 5), this interpretation is more than justified by the law of probability. From such considerations, Lewis concluded that the *Q–R–S* group of the biogram has the following factors: *Q* and the chief portion of *R* are right-sided events in Leads II and III but left-sided in Lead I; *S* is a right-sided event in Lead I but left-sided in Leads II and III.

It is obvious that according to this interpretation the *Q–R–S* deflection is not associated with conduction through the Purkinje arborization, but is coincident with and due to the passage of the impulse from the endocardial to the epicardial surfaces of ordinary ventricular muscle.

Moreover, quite contrary to generally accepted facts, this conception indicates and emphasizes that the negative deflection, *S*, is not associated with apical but with basal activity. In other words, the direction of the deflection is determined, not by assumed distributive potential differences between the base and apex, as a whole, but rather by the direction of *limited potential differences*[1] arising during the spread of the excitation process. When the direction of the electrical axis is, in the main, downward the basal contact is relatively negative; when it is mainly upward, irrespective of whether the limited potential differences occur at the base or apex, the basal contact becomes positive.

As regards the interpretation of the *T* wave, expressions have generally been much less definite. They may be grouped into four divisions: (1) That the *T* wave is not really indicative of any potential change due to activity of the muscle but to changes in the position of the heart (Usoff) or to changes in electric stress (Meyer); (2) that it is the result of a contraction in certain regions or layers of muscles; (3) that it is not a special feature associated with contractions from any particular region but a phenomenon occurring at the end of the entire contraction process in the ventricle. The first of these views has not been very generally supported. The second view has been largely supported by many investigators but differently interpreted. Gotch, Kraus and Nicolai and others incline to the belief that the spread of contraction is so ordered that the basal portions of the heart are last affected and so continue in the contracted state later. Bayliss and Starling, as well as Einthoven, seem inclined to the belief that the terminal basal negativity does not represent a return of the contraction wave, but a continuation of negativity after it has disappeared elsewhere. Lewis has attempted to give this view a clearer statement, and one that may consistently be held in the light of our recent knowledge regarding the spread of the excitation period. According to

[1] For detailed discussion as to the conception of distributed and limited potential differences, *cf.* Lewis: Arch. Int. Med., 1922, **30**, 269.

Lewis, changes in activity within the ventricles may be described as consisting of: (1) A stage of invasion, during which the excitation wave is spreading; (2) a stage of possession, in which a condition of isopotential is found in all parts of the contracting muscle; (3) a stage of retreat, during which contraction subsides in the order in which muscle fractions were excited. Electrical variations associated with the offset of the contraction process occur more slowly than those associated with the onset of excitation, therefore the *T* wave may be interpreted as associated with the last two stages. As "invasion" and "retreat" follow more or less the same paths when the heart beats naturally and as the basal portions of the ventricular walls are the last to be excited, according to studies of the dextro- and levocardiograms (*cf.* Fig. 94, *C*), it is likewise probable that they remain contracted somewhat longer. This relatively negative potential at the base would then account for the positive character of the final *T* wave. The third view that the *T* wave is representative of muscular contraction irrespective of position was first suggested by Hoffmann and has been supported by numerous observations. In the first place, the *T* wave is not peculiar to ventricular contraction, but has been recorded by sensitive galvanometers from the auricles, ventricular strips and the aortic conus of both amphibian and mammalian hearts (Bakker, Eiger, Straub, Meek and Eyster, Guthrie[1]). To explain its upward deviation it is necessary to assume a preponderance of contraction on one side of the equipotential line. Whether the wave moves in the same or opposite direction as *R* will, therefore, depend on a balance between the action current produced by the contracting muscles on each side of this line. The actual direction in electrocardiograms will, therefore, seem to depend on: (1) The line of equipotential in relation to any given lead; (2) the extent of contraction of the ventricular muscle as a whole; (3) the relative degree of contraction in the basal and apical portions of the ventricle (Eyster and Meek).

FACTORS DETERMINING AMPLITUDE AND DIRECTION OF DEFLECTIONS IN DIFFERENT LEADS.

While in the majority of normal individuals the general character and sequence of contractions are quite similar in the three leads, the relative amplitudes of homonymous waves are quite different. Under abnormal conditions these differences may become much exaggerated and the direction of the deflections may, indeed, no longer correspond in all leads.

Multiple Indirect Leads from a Muscle Sheet.—In discussing the cause of these differences, we may begin with a simple case illustrating the importance of taking multiple indirect leads. Let us suppose a

[1] Unpublished experiments on ventricular strips. (Personal communication.)

flat sheet of muscle, *A B C D*, to be immersed in a saline bath and that we lead off from the ends of the vessel, *E F*, and from the sides, *G H* (Fig. 95, *I*). For brevity, let us call these Leads I and II respectively. Let us now consider the effects when an impulse passes not as a cross-sectional wave but in all directions from a point. It is obvious that if the wave originates at a medial point, *M*, the paired surfaces *E* and *F* as well as the paired surfaces *G* and *H* will be negative simul-

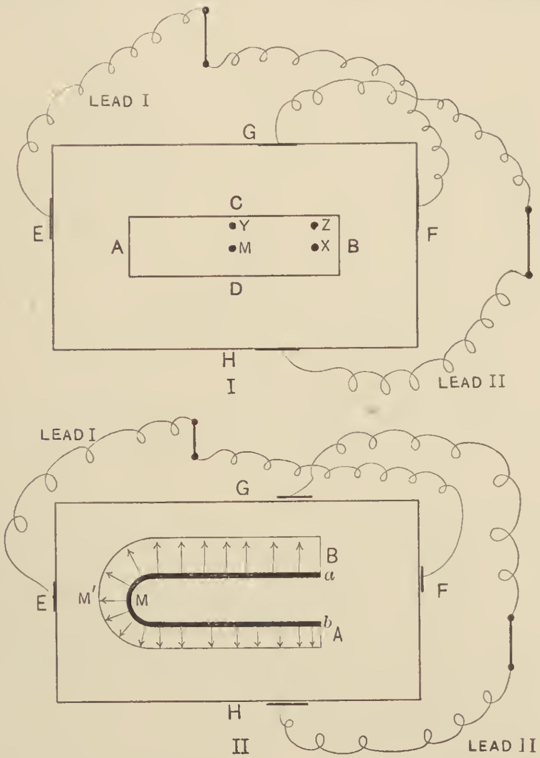

FIG. 95.—Diagram illustrating significance of different leads. *I*, illustrating the influence on electrical deflections from different leads when impulses spread radially from a single point in a muscle strip (modified after Fahr); *II*, illustrating the influences on deflections derived from different leads when impulses spread in U-shaped muscle strips similar to that of heart. (Modified after Wilson and Herrmann.)

taneously, and no current will be recorded by either lead. If the excitation rises from *X*, sides *G* and *H* again will be simultaneously negative, but *F* will be negative before *E;* consequently, a current is recorded by Lead I but none by Lead II. The reverse is the case when the excitation spreads from *Y*, which is equidistant from *E* and *F*, but nearer to *G* than *H*. Finally, if the excitation arises from *Z*, a point nearer to both the sides *F* and *G*, a current from both leads is

obtained. A little reflection will show, moreover, that the contour and amplitude of the deflections recorded by Leads I and II may be entirely different. These simple considerations should make it evident that: (1) Unless the leading-off electrodes are in line with the spread of negative potential no current is detected by indirect leads; (2) when potential variations occur in several directions entirely different curves will be recorded from different leading-off points.

The Components of Complex Derivations.—Let us now suppose that instead of a sheet of muscle we have a U-shaped strip, as shown in Fig. 92, *IV*. As already explained, when the whole cross-section of this strip is stimulated at M or simultaneously at A and B the leading-off electrodes from sides E and F will yield a simple diphasic current. Such a loop has often been compared to the ventricles, which with their left and right outer walls also form a similar loop. In such a case M would represent the apex and A and B the base. The ventricles are not excited in this fashion, however, but more nearly as is shown schematically in Fig. 95, *II*. Let us suppose that the excitation arises at a point, M, on the inner side of the U and that from this point it spreads rapidly to the ends, a and b, along a thin inner band of tissue represented in the diagram by a heavy line. Further, let us suppose that from this line it spreads crosswise through the muscle at a much slower rate, as is indicated by the arrows. Under such conditions two factors may conceivably influence the deflections derived from Lead I, viz.: (a) The rapid spread of negativity from M to a and b may cause E to be negative before F and so produce an initial negative phase; (b) the slower spread of current from M to M^1 may cause F to be negative before E and so produce a positive initial deflection. We cannot as yet be certain what influence predominates, but from the fact that the spread along the inner band occurs with such great velocity and involves so small a quantity of muscle tissues the probabilities are that the passage of the impulse from M to M^1 determines the resultant deflection.

Considering now the variations recorded from Lead II of our diagram, it is obvious that neither the passage of the impulse through the inner layer nor its passage through the region M–M^1 will affect the potential of sides G and H. They are affected, however, by currents passing through B toward G and through A toward H, and it is at once obvious that the directions are opposite. Assuming that A and B are of equal thickness and that they propagate impulses at equal velocities, G and H will be simultaneously negative and no deflections will be recorded by Lead II. If, however, impulses pass across A slightly in advance of B or if limb B is appreciably thicker, as represented in the diagram, side H is primarily negative and side G predominantly negative somewhat later, thus giving a diphasic variation in current.

A little consideration will further show that in the latter case the

recorded deflection represents a biogram consisting of the algebraic sums of the negative variation in A and in B. By preventing the passage of the impulse first to A and later to B, it is possible to record variation currents separately, which when algebraically added give a replica of the original in Lead II. This, it must now be evident, is the principle upon which Lewis was able to determine that the electrocardiogram is a biogram, which is separable into a dextro- and levo-electrocardiogram (*cf.* page 273).

Surface Leads from Triangular Areas.—Previous discussion should have made clear the following proposition, viz.: (1) The direction and magnitude of the *actual potential differences,* which can be derived from a complicated contracting muscular mass *at any moment,* is the resultant of all the potential differences taking place during that moment; (2) that the deflections recorded by indirect leads are further affected by the relation that the direction of the *actual potential differences* bears to the direction of the leads at different moments.

As the heart is an organ of three dimensions, however, the direction of this line of *actual potential difference* does not lie in the frontal plane of the body, from which, however, we lead off in our usual procedure. We can, therefore, only hope to record a frontal projection of this *actual potential difference,* which Einthoven has called its *manifest value.* Fortunately, as Einthoven has postulated, the manifest value bears a constant relation to the actual potential difference and changes in exact ratio to it during different phases of the cardiac cycle.

This manifest potential may be recorded from the anterior body surface when the frontal leads are placed parallel to its general direction. Thus, if the manifest current be represented both in magnitude and direction by the line x–y (Fig. 96), the leads must be placed parallel to this line. This has led Einthoven to define the *manifest value* of the potential differences as that value which is found in a lead taken from electrodes placed parallel to its general direction.

In taking leads from the limbs we are in reality recording from lines represented by a triangle, $R\,A$, $L\,A$, L, none of which are parallel to the line of manifest potential, $x\ y$. Consequently, we are not obtaining the full manifest value in any lead, but only such an amount as may be measured by projecting the arrows, $x\ y$, perpendicularly to the three sides of the triangle. In other words, if $x\ y$ represent the direction and magnitude of the manifest potential, the differences $x_1\ y_1$–$x_2\ y_2$–$x_3\ y_3$ represent the relative magnitude of R deflections recorded in Leads I, II and III respectively.

According to this conception, *we should expect the waves recorded by Lead II to be larger than those from Lead I, and these, in turn, larger than those from Lead III.* That this is, as a rule, actually the case in normal hearts is shown in the three leads of Fig. 90. Einthoven and Fahr have shown mathematically that Lead II equals Lead I plus

Lead III, provided account is taken of the fact that the waves in Leads II and III start earlier than those in Lead I, while the summits are recorded later than in Lead I.[1]

The direction of the waves in any lead depends on the direction of the electrical axis in the heart. If x–y (Fig. 96) represents the direction of the flow in the heart and the dotted lines its distribution and direction in the tissues then the flow in Lead I will be from *LA* to *RA*, in Lead II from *L* to *RA*, in Lead III from *L* to *LA*.

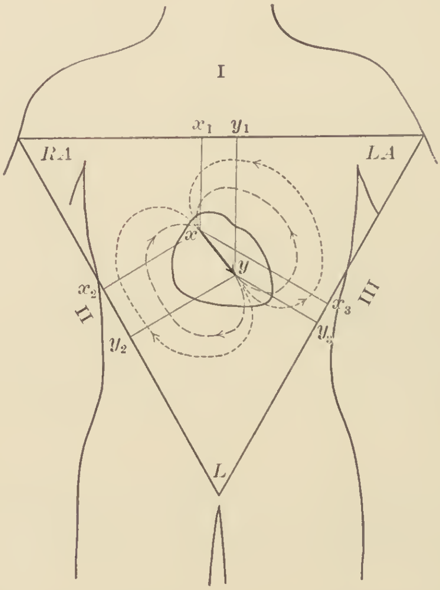

Fig. 96.—Diagram showing relations of the electrical axis of the heart to the three leads. *RA*, right arm; *LA*, left arm. Roman numerals refer to leads. (After Pardee.)

Now, if the current represented by *xy* flows in a horizontal direction, as shown in Fig. 97, *A*, then, as normally, the current would flow in Lead I from *LA* to *RA*, in Lead II from *L* to *RA*, as is normally the case; but in Lead III, from *LA* to *L*.

Again, if the current represented by the line *xy* flows downward parallel to Lead III, then (Fig. 97, *B*) the current will flow in Lead II from *L* to *RA* and in Lead III from *L* to *LA*, as is normally the case; but in Lead I it will flow from *RA* to *LA*. Since in left- and right-sided hypertrophy, as well as under abnormalities of bundle branch

[1] Corresponding points on the *R* wave may be obtained by recording at least two electrocardiogram leads simultaneously or by relating consecutive leads to some specific dynamic event recorded simultaneously. For this purpose the synchronous records of heart sounds are especially to be recommended.

conduction, the electrical axis of the heart is changed, it is possible, on the basis of such applications, to diagnose these conditions.

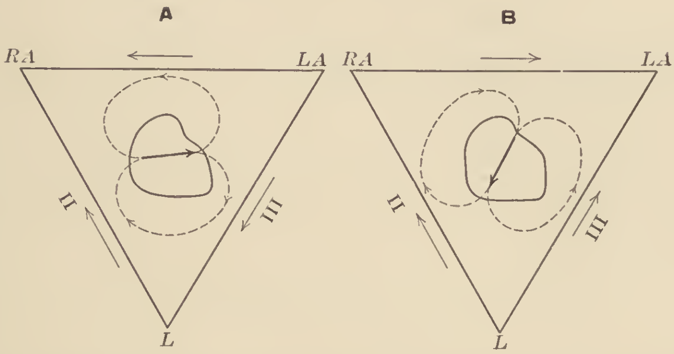

FIG. 97.—Diagrams showing how abnormal "electrical axes" in the heart cause different deflections in various leads, lettering same as before. (Modified slightly after Pardee.)

The Calculation of the Electrical Axis and Manifest Value.—Before proceeding it should be emphasized that both the magnitude and direction of the manifest potential value, x–y, changes constantly during the cardiac cycle and that consequently calculations may be made for each wave of the electrocardiogram. These may be desig-

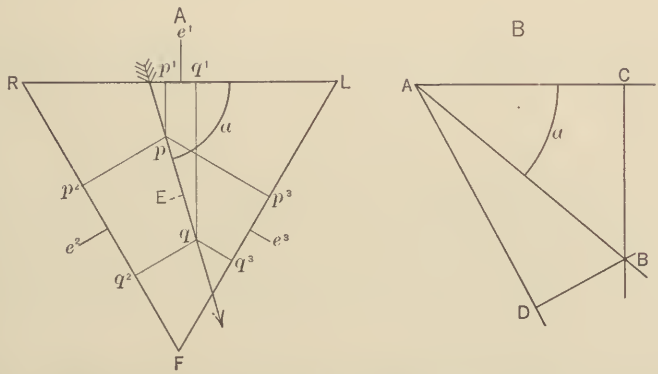

FIG. 98.—Diagrams illustrating methods of determining the direction of the electrical axis and manifest value. *A*, manifest values after method of Einthoven, Fahr and Waart; *B*, according to method of Fahr.

nated by the letters R_m S_m T_m, etc. Inasmuch as the most significant alteration of the electrocardiogram under abnormal conditions affects the *R* wave, however, *calculations of the electrical axis and manifest value are ordinarily limited to* that stage of the cardiac cycle which corresponds to the *R* deflection.

Several different procedures have been suggested for calculating the electrical axis and manifest value. The original method of Einthoven is as follows: An arrow is drawn through the mid-point of the equilateral triangle, *R F L* (Fig. 98, *A*), and this arrow makes an optional angle, a, with the side, *R L*. On this arrow a line $p\,q$ of optional length is taken. The projections of $p\,q$ to the sides of the triangle are $p^1\,q^1$, $p^2\,q^2$ and $p^3\,q^3$. If E is the manifest potential difference developed along the line of the electrical axis and e^1, e^2 and e^3 are the potential differences, as they are represented in the sides of the triangle, then the values of e^1, e^2 and e^3 are proportional to the lines $p^1\,q^1$, $p^2\,q^2$ and $p^3\,q^3$ and:

$$e^1 = E \cos a \tag{1}$$
$$e^2 = E \cos (a - 60°) \tag{2}$$
$$e^3 = E \cos (120° - a) \tag{3}$$
$$e^3 = e^2 - e^1 \tag{4}$$

When a is unknown it can be calculated from the relations of any two of the potential differences.

$$\text{Using } e^1 \text{ and } e^2 \text{ we derive the formula } \tan a = \frac{2e^2 - e^1}{e^1\sqrt{3}} \tag{5}$$

$$\text{Using } e^1 \text{ and } e^3 \text{ we derive the formula } \tan a = \frac{2e^3 + e^1}{e^1\sqrt{3}} \tag{6}$$

$$\text{Using } e^2 \text{ and } e^3 \text{ we derive the formula } \tan a = \frac{e^2 + e^3}{e^2 - e^3}\sqrt{3} \tag{7}$$

The calculation of the manifest value, E, which has been taken arbitrarily as the distance $p\,q$, may then be calculated from the formula:

$$E = \frac{e^1}{\operatorname{Cos} a} = \frac{e^2}{\operatorname{Cos} (a - 60°)} = \frac{e^3}{\operatorname{Cos} (120° - a)} \tag{8}$$

In order to apply this method it is necessary to determine the potential differences in millivolts from two leads at fixed points in the cardiac cycle. Thus suppose that R_{II} deflection to the summit is 10 millivolts and a point on the R_{III} wave occurring in exactly the same phase of the cardiac cycle (not necessarily the summit) is 5 millivolts then from the formula (7), given above—

$$\tan a = \frac{10 + 5}{10 - 5}\sqrt{3} = 3\sqrt{3} = 1.732$$

As the tangent of 1.732 is a 60-degree angle the *electrical axis at that phase of the cycle is inclined* 60 *degrees to the horizontal.*

Applying further either the second equation of formula (8)—

$$E\text{, the manifest value} = \frac{10}{\operatorname{Cos} (60° - 60°)} = 10$$

or applying the third equation of (8)—

$$E = \frac{5}{\text{Cos}\,(120° - 60°)} = \frac{5}{0.5} = 10$$

Within recent years a number of simplified procedures based on the Einthoven triangulation method have been suggested. The method of Fahr is as follows: An angle of 60 degrees is constructed (*C A D*, Fig. 98, *B*). Along the horizontal side of the angle a distance equal in centimeters to the value of Lead I in tenths of millivolts is laid off. Along the other side of the angle a distance is laid off, whose length in centimeters equals the synchronous value of Lead II in tenths of millivolts. Perpendiculars, *C B* and *D B*, are dropped from these points. The point of intersection, *B*, is connected with the vertex of the angle. The length of line *A–B* in centimeters gives the potential difference corresponding to the "manifest value" for this moment in the cardiac cycle. The direction of this line gives the direction of the resultant electromotive force present in the heart at this moment and the angle formed by this line with the horizontal line is the angle a.

In order to avoid the calculation or construction entailed by these triangulation methods, a number of investigators (Pardee, Carter, Richter and Greene, Lewis, Wilson and Herrmann, Mann, Dieuaide) have constructed charts, by means of which the electrical axis may be more rapidly determined. For the details of these charts the original reference should be consulted.

CLINICAL ASPECTS OF THE ELECTROCARDIOGRAM.

In spite of the fact that electrocardiography has been introduced into clinical use only within comparatively recent years, its field of activity is no longer restricted to scientific and experimental work, but it has become an important and often indispensable aid in establishing the diagnosis, prognosis and management of cardiac disorders. This is due to the fact that we possess sufficient results from which it is possible to state, with a considerable degree of surety, that certain pathological disturbances are associated with definite variations in the size, contour and time relations of the individual waves.

Normal Variations.—Before it is possible to interpret the waves characteristic of pathological conditions, it is desirable to know what variations may be considered within the range of normal. Many investigators have made such studies in normal persons. As a result, it has been found that the normal electrocardiogram does not change in the same individual for long periods of time. The contour and time relations of the different waves are generally so characteristic that they can be picked out at a glance. On the other hand, variations in the different waves do occur in different individuals.

The *P* wave is usually a small rounded wave, reaching its summit in 0.03 to 0.04 second and in a slightly shorter time returning to zero potential. Occasionally the summit is flattened, notched or bifurcated. Again, it may be scarcely recognizable or even negative in one lead (usually Lead III). A negative *P* wave (Fig. 99) is quite generally regarded as indicating a shifting of the pacemaker from the head of the *S–A* node to an inferior location (Einthoven, Lewis, Eyster and Meek). As such a condition may be experimentally produced in

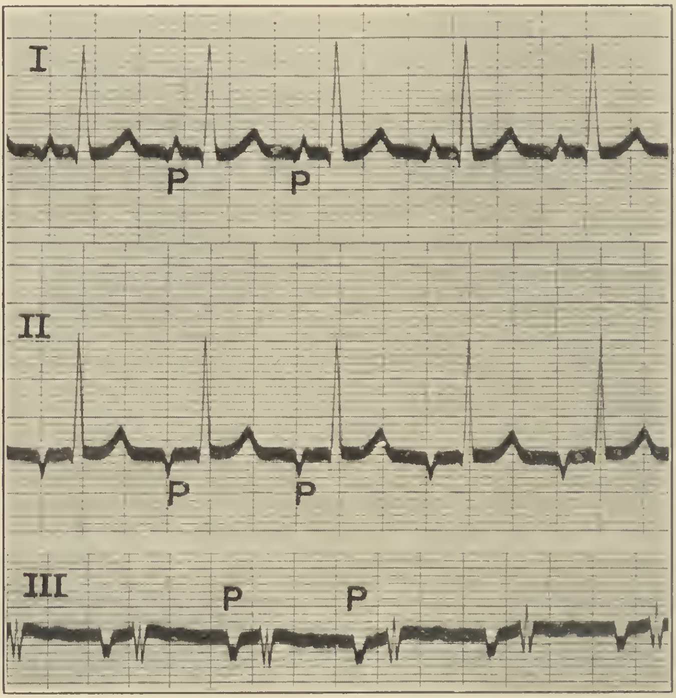

Fig. 99.—Three electrocardiogram leads showing negative *P* waves in Leads II and III, responsible at intervals for recurrent attacks of auricular tachycardia, and indicating origin at abnormal focus. Lead III also shows small splintered *R* waves entirely negative during expiration. (Courtesy of Dr. R. Scott.)

animals by vagus stimulation, it is also probable that a similar functional cause may determine the change in pacemaker in man. In favor of this interpretation are the observations that in some individuals negative *P* waves appear after digitalis medication (Carter and Wedd) and as a result of deep inspiration (Wilson), whereas they become positive after the use of atropine.

In other cases the waves, however, seem to remain negative after atropine and do not change on vagus compression. It is doubtful,

however, whether such subjects may be regarded as having a pathological involvement of the *S–A* node; indeed, it is more probable that it may be explained, as Carter and Wedd suggest, by a change in the balance of electrical variation which alters the relation of the pacemaker to the axis for the derivation of the lead in which they appear. Unless inverted waves are associated with reduced or reversed *P–R* intervals (Fig. 145) or are accompanied by auricular extrasystoles (Hamburger) or periodically give rise to tachycardia, as was the case in Fig. 99, they cannot be regarded as indicating any pathological process in the *S–A* node. It is further significant that inverted *P* waves occur most frequently in Lead III alone. Thus, Goddard in 700 cases found that the *P* wave was inverted only 4 times in Lead I, 7 times in Lead II and 75 times in Lead III. Fig. 99 shows an instance where this wave is negative in Leads II and III but upright in Lead I.

The ventricular complex may or may not be inaugurated by a negative *Q* depression. Kraus and Nicolai state that the *Q* depression was present in approximately one-third of their cases. Out of the 59 cases examined, Lewis and Gilder observed its presence in 37 cases in Lead I, 45 cases in Lead II and in 36 cases in Lead III. Its average depth, measured from the zero level, was somewhat greater than the height of the *P* wave. The *R* wave is characterized by its steep rise and sharp point and is a useful guide to early ventricular events. Its rise begins from 0.12 to 0.18 second after the rise of the *P* wave. The *P–R interval* is theoretically the most exact estimate we have of the time taken for the impulse to be conducted from the *S–A* node to the ventricle. It varies considerably, however, in different leads, due to the fact that corresponding waves do not rise simultaneously. This is well illustrated in curves published by Williams, in which $P_{\text{I}} - R_{\text{I}} = 0.13$; $P_{\text{II}} - R_{\text{II}} = 0.17$ and $P_{\text{III}} - R_{\text{III}} = 0.18$ second. The *S* depression is sometimes lacking, especially in Lead III, where Lewis and Gilder observed its presence in 31 out of 59 apparently normal cases; it may, however, be unusually deep.

The duration of the entire *Q R S* complex varies in different individuals, but usually occupies an interval of about 0.03 to 0.04 second (Lewis, Einthoven). Most electrocardiographers regard 0.1 second as the extreme lengthening, which may still be considered normal (Lewis, Carter, Robinson, Oppenheimer and Rothschild, etc.). The height of the various waves varies slightly with the heart rate and respiration in separate leads, but, on the whole, the *Q R S* complex is largest in Lead II and smallest in Lead III.

The final *T* wave is a rounded deflection and follows a phase of isopotential. It is from one-fourth to two-fifths the size of *R* in Lead II, whereas in Lead III the wave may be negative. The *U* wave following the *T* wave was present in three-fourths of Lewis and Gilder's cases, and in fully one-half of the records obtained by Einthoven. It is most frequently present in Lead II, and is always very small,

The following table taken from Lewis and Gilder, showing the average height of the waves, expressed in millivolts, may be of interest:

Lead.	P.	Q.	R.	S.	T.	U.
I	0.52	0.51	5.16	2.06	1.93	0.07
II	1.16	0.73	10.32	2.23	2.46	0.16
III	0.81	0.86	6.61	1.73	0.61	0.06

The following percentile relation in Lead I, given by Linetzky, is a rougher statement of the relative height, but a convenient one to bear in mind:

$$P : R : S : T = 10 : 100 : 5 : 20$$

Variations in the Q R S Complex.—A number of interesting variations of the initial complex occur in apparently normal individuals. Among the most frequent of these are a small or inverted complex in Lead III or an isoelectric line during the *Q R S* interval. The latter occurs most frequently in Lead III, but may be present in any other lead. It may change from time to time in the same individual (Carter and Dieuaide). Such effects are probably of no pathological significance and due to the particular electrical axis present in the heart at that time. An analysis of the data obtained by Einthoven's triangulation method shows that the leads may change their direction rapidly from + to − or reversely when the electrical axis lies at the following angles: For Lead I at +90 degrees and −90 degrees, for Lead II at +150 degrees and −30 degrees and for Lead III at +30 degrees and −150 degrees. When the electrical axis at the time of the initial deflection lies close to one of these angles the corresponding lead becomes approximately zero (Carter), and the reason that Lead III most commonly shows a line of isopotential or a negative initial complex is due to the fact that normally the electrical axis of the heart *at the time of the R wave* lies between +30 degrees and +70 degrees. Slight differences in the direction of the electrical axis due to position changes in the heart may, therefore, produce marked variations in the *Q R S* complex of Lead III.

Another frequent variation consists of a splintering or notching of the *R* wave. Lewis and Gilder were the first, I believe, to emphasize its frequency in Lead III, and this has been repeatedly confirmed (Fig. 99). Such splintering always occurs in waves of small amplitude (commonly Lead III) and, while it may appear either on the ascending or descending limb, it is always near the base line. Such splintering depends probably on the manner in which the electrical axis shifts and the way in which the dextro- and levo-electrocardiograms are summated. It is, therefore, probably without significance, but must be carefully distinguished from the notching or splintering which occurs near the apex of very large deflections (Fig. 164), which is indicative of definite conduction disturbances (Wilson and Herrmann).

Effect of Respiration.—The actual and relative size of the waves may vary with the phase of respiration. Einthoven believes that this is due neither to an action current developed by the contraction of the respiratory muscles, nor to a changing resistance occasioned by enlargement of the chest. The nature of the changes depends on whether or not the heart is rhythmic. When the length of the cycle varies greatly it determines the effect on the individual waves. In the long cycles the P wave is smaller, especially in Lead III; R is larger and T smaller in Leads I and II; but R is also smaller in Lead III (Hoffmann). When the heart rhythm is regular the R and T waves generally become smaller during inspiration in Lead I but larger in Lead III. Occasionally, however, the respiratory effects are reversed, R_{I} increasing during inspiration and R_{III} decreasing (Carter and Dieuaide). Occasionally a negative R_{III} may be produced by a deep inspiration. These effects are all due to the changing position of the heart during inspiration and expiration, which also affects the resultant electrical axis. This is illustrated by the following figures calculated from these respiratory variations by Waller:

Position.	Angle of electrical axis. Inspiration.	Expiration.
Standing	29°	45°
Sitting	40°	53°
Lying on back	39°	50°

Effect of Body Position.—The position of the body modifies the waves. The S wave becomes larger when the body is shifted from the left to the right side. A change from a dorsal to a stomach position induces the same effect as expiration, probably because the diaphragm is pushed up. Slight changes in the waves often follow a change from a reclining to an upright sitting position. Sitting acts similarly to expiration by compressing the abdomen and causing an upward movement of the diaphragm. No difference in the record occurs between the "lying down" and the "propped-up" positions in bed (Einthoven). A decrease in the amplitude of R_{III} or even a negative initial complex may result in a change from the "back" to the "left lateral" position (Carter and Dieuaide).

Normal Electrocardiograms in Children.—Electrocardiograms of normal children of various ages have been reported upon by a number of investigators, among them Nicolai and Funaro, Lewis, Hecht, Noeggerath, Krumbhaar and Jenks, Linetzky, Seham, etc. The results show fairly concordantly that during the early period of infancy the initial deflections in Lead I are negative, indicating that the musculature of the right heart is predominantly more developed than in adults. Between the second and third months, however, the electrocardiograms gradually begin to change, R being directed upward in Lead I, though still followed by a deep S depression. After six months the deep S depression also tends to disappear and adult types of

electrocardiograms are obtained. Among the other deviations from the adult type that have been noted in early life are: A higher *P* wave in all leads, a deeper *Q* wave (especially in Leads II and III) and the absence of the *P* wave in Lead I during the first ten days. The *P* wave is rarely inverted in early life, but becomes so in about 15 per cent of cases observed in later childhood. (For literature and illustrations, *cf.* Seham.)

PATHOLOGICAL VARIATIONS.

The Significance of Abnormal Initial Complexes.—Since the initial complexes recorded by the three customary leads are algebraic additions of contrarily directed currents through the right and left ventricles (*cf.* page 273), a large variety of abnormal complexes may occur when the two ventricles are excited at different times or through different routes than those normally followed. This follows particularly whenever a complete or partial block occurs anywhere and beyond the common *A–V* bundle or when premature impulses arise in irritable foci within the right or left ventricles.

Complexes Regarded as Characteristic of Bundle Branch Block (*cf.* Fig. 164).—Experimental work as well as clinical studies by postmortem examination indicate that complete block of one bundle gives rise to aberrant complexes characterized: (*a*) By the large size and broad base (0.15 to 0.25 second); (*b*) by the notched, splintered or broadened summits; (*c*) by their reversal in certain leads. Right-bundle branch block is usually regarded as indicated when the aberrant deflection is downward in Lead III, left bundle branch block when it is directed downward in Lead I (Fig. 164, *A*, *B*). In such cases, moreover, the large positive initial deflections are followed by deep negative *T* waves, while the larger negative initial deflections are followed by large positive *T* waves. (For more detailed analysis and the correlation with animal experiments, *cf.* page 500.)

Complexes Regarded as Characteristic of Arborization or Intraventricular Block.—When the initial complexes are relatively small instead of large, show a slighter degree of widening (*i. e.*, when the *Q R* interval exceeds 0.1 second somewhat) and, in addition, the waves are splintered or abnormal in appearance (Fig. 149), it is probable that the excitation of the ventricle does not occur normally. Since these deflections are quite unlike those obtained in frank bundle branch block, and as they are often found on postmortem examination to be associated with patchy sclerosis in the subendocardial layers of the ventricle, the suggestion was advanced by Oppenheimer and Rothschild that they are characteristic of arborization or intraventricular block, a view that has subsequently received support from Neuhof, Willius, Carter and Wedd. Statistics, furthermore, seem to indicate that a higher mortality occurs in cases presenting such deflections

(70 per cent) and that the average life expectancy is about eight and a half months (Willius[1]).

Since aberrant deflections are sometimes obtained from individuals who on postmortem studies do not show endocardial degeneration, since, moreover, the waves may revert to normal under the influence of digitalis and rest (Robinson), and, finally, since experiments have shown that alteration in the oxygen supply, accumulation of lactic acid and other metabolic products may definitely modify the conduction through the ventricles, Robinson suggested that these abnormal waves do not necessarily presage degenerative changes in the myocardium, but may be caused by functional disturbances alone.

The possibility must still be admitted, however, that such characteristic deflections may give no indication whatsoever of arborization or intraventricular block, either functional or anatomical (Wilson and Herrmann). Experimental work, in which extensive lesions of the arborization were produced, shows no evidence of similar changes in the *Q R S* deflections (Smith, Wilson and Herrmann). Wilson and Herrmann, on the basis of probability as well as animal experiments, therefore, incline to the view that these deflections are caused by incomplete bundle-branch block rather than by arborization or intraventricular block. (For further analysis, *cf.* page 504.)

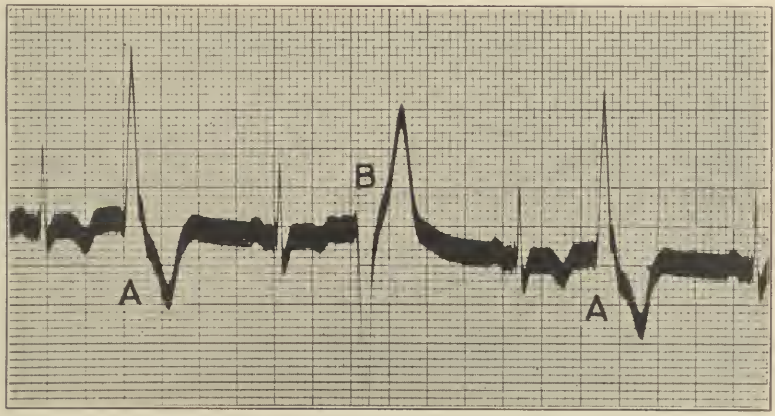

Fig. 100.—Electrocardiogram (lead *III*) showing two premature right-sided systoles (*A*) and a premature left-sided systole of the ventricle (*B*) interposed between normal complexes. (Kindness of H. B. Williams.)

Complexes Characteristic of Ventricular Premature Systoles.—When one ventricle is excited before the other the initial complexes differ from normal in that they are much larger, occupy a longer time interval and are followed by a marked negative depression (Fig. 100).

[1] In a more recent analysis Willius found that when aberrations of *Q R S* are present in all three leads, 62 per cent of cases live less than 14.2 months.

When the right ventricle is excited before the left the waves are directed upward in Leads II and III but downward in Lead I; while if the left ventricle is excited first, they are positive in Leads I and II and negative in Lead III.

Complexes Regarded as Characteristic of Right or Left Ventricular Preponderance.—Einthoven, on the basis of records obtained from cases of aortic disease and mitral stenosis associated with left and right ventricular hypertrophy, respectively, postulated: (*a*) That in hypertrophy of the right heart the initial deflection is downward in Lead I and exaggerated and upward in Lead III; (*b*) that in left ventricular hypertrophy the large initial deflection is downward in Lead III and upward in Lead I (*cf.* Fig. 190). The fundamental reasons for these changes have already been analyzed (*cf.* page 279), and it need only be reëmphasized that this is not due to any difference in the mode of generation of the current by the heart, but to the fact that when one ventricle enlarges there is a change in the electrical axis of the heart.

Almost conclusive evidence is now available (*cf.* page 574 for detailed discussion) that, while the electrocardiogram does not necessarily indicate whether one ventricle or the other is hypertrophied alone, it is the most satisfactory sign as to the ventricle which has undergone a predominant increase in muscle mass (*cf.* Lewis, Carter and Greene, Wilson and Herrmann).

Differentiation between Hypertrophy and Bundle Branch Defects.—Inasmuch as both bundle-branch defects and one-sided ventricular preponderance cause inverted waves either in Leads I and III, their differential diagnosis must be briefly considered (*cf.* Figs. 164 and 190). As a rule, the character of the initial deflections is sufficient; in hypertrophy the inverted waves are normal in contour and duration while in bundle lesions they are broader and of abnormal contour, being frequently notched or splintered, as already indicated. Furthermore, the direction of the terminal, deflection *T*, may serve to distinguish the two conditions. In hypertrophy the *T* deflection occurs in the same direction as normally, while in bundle-branch block the *T* variation is directed opposite to initial complexes. Finally, the *Q R S* deflection of Lead II is less frequently negative in left preponderance curves than in right bundle-branch block.

Difficulty in interpretation arises, however, as soon as one-sided preponderance and either complete or incomplete block of one bundle are associated. Furthermore, there are transitional records, in which a differential diagnosis—between left ventricular preponderance and right bundle-branch block, for example—is quite impossible (Wilson and Herrmann). Such records show *Q R S* intervals of 0.15 second, are often slightly notched and have the *T* deflection in the opposite direction.

Significance of Inverted T Waves.—As already indicated, the *T* wave is often inverted in normal individuals in Lead III, consequently

no pathological significance can be attached to such isolated occurrence. The T wave, moreover, becomes inverted in all leads as a result of early digitalis intoxication. Moreover, as above analyzed, T may be inverted in Leads I and II after abnormal initial complexes, due to bundle-branch defects or to premature ventricular contractions.

When the effects of digitalis medication can be excluded and negative T waves recur regularly in several leads, particularly in Leads I and II, serious involvement of the myocardium may be diagnosed with a fair degree of accuracy (*cf.* also page 294). Mortality studies indicate that the period of life expectancy is greatly reduced. Thus, Willius reports the following mortality as compared with normal controls:

T wave negative in	Mortality.	Controls.
Leads I and II	65.0 per cent in 12.7 mos.	17.0 per cent in 10.8 mos.
Lead I	63.4 per cent in 8.5 mos.	26.0 per cent in 2.4 yrs.
Leads I, II and III	62.5 per cent in 12.7 mos.	20.5 per cent in 19.2 mos.
Leads II and III	32.3 per cent in 11.0 mos.	20.0 per cent in 1.5 yrs.
Leads I, II and III with Q–R–S aberrations	86.7 per cent in 12.7 mos.	

Changes in Electrocardiograms during Arrhythmias.—In addition to the changes in the contour of the initial deflections resulting from a number of different conditions giving rise to cardiac irregularity, the electrocardiogram is of value in several other ways in determining the nature of the irregularity.

1. *The waves may be present in their normal sequence but with altered time relations.* Thus, it is possible to state that the conduction time from the S–A node to the ventricle is greater when the P–R interval in Lead II is greater than 0.2 second (Fig. 166). During infections a lengthening of the P–R interval may be the first evidence of involvement of the cardiac muscle. In sinus irregularities and tachycardias the waves follow in proper sequence, but their rhythm or rate is altered.

2. *The sequence of waves may be altered.* Thus, in A–V nodal rhythm the R deflection may precede the P wave, as shown in Fig. 145.

3. *Certain waves may be absent or present in excessive number.* Thus, in auricular flutter (Fig. 154), when the auricle may attain a rate of 200 or 300 per minute, the number of P waves between the preceding T and following R are greatly increased, while in auricular fibrillation (Fig. 155) the typical P waves are absent.

Summary of Typical Features of the Electrocardiogram in the More Common Forms of Irregularity.

While the chapters dealing specifically with the various types of arrhythmia should be consulted for details, the following summary of the more important features associated with ordinary and simple forms of irregularities may be of value.

A. Sinus Arrhythmia.—The electrocardiogram consists of a normal sequence of *P*, *R* and *T* waves in all leads, but the cycles are not of uniform length. The increase and decrease in cycle length may be progressive or may occur abruptly. Occasionally the *P* and *R* wave become smaller in the more rapid cycles.

B. Sino-auricular Block (Fig. 160).—In the normal sequence of *P*, *R* and *T* deflections, both auricular and ventricular complexes suddenly fail for an interval corresponding approximately to that of a normal cycle. These omissions of complexes may occur occasionally or become permanent, resulting in a halving of the number of recorded complexes.

C. Auricular Premature Contractions (Fig. 146).—An otherwise regular rhythmic sequence of *P*, *R* and *T* deflections is upset by the premature occurrence of an entire group of waves followed by a longer phase of isopotential. The *P* wave may resemble but is never quite identical in appearance with the normal *P* waves unless the premature contraction arises very near the *S–A* node. It is inverted when the premature stimulus arises in lower structures. There are no essential changes in the ventricular complexes.

Occasionally a premature auricular systole is blocked. In such a case a premature *P* wave occurs without succeeding ventricular complexes. If the premature auricular contraction comes late in ventricular systole the *P* wave may deform or be superimposed upon a preceding *T* wave. When premature contractions arise in the *A–V* node or nodal junction the *P* waves may be closely followed by an *R* deflection, *i. e.*, the *P–R* interval is greatly reduced. Again, they may be incorporated within the *R* complex, indicating that auricular and ventricular contractions occur simultaneously.

D. Ventricular Premature Contractions.—Waves of large amplitude and broad base followed by *T* waves of opposite potential are characteristic of ventricular premature contractions (*cf.* Fig. 100). If the excitation arises in the right ventricle the waves are directed downward in Lead I but are upward in Lead III; if the excitation arises in the left ventricle the large deflection is directed downward in Lead III and is positive in Lead I. A large variety of forms exist in which this direction of the deflections in Lead I is not observed. Thus, in many right-sided premature systoles the deflection may be positive both in Leads I and III; occasionally it is negative both in Leads I and II. On the other hand, in left ventricular extrasystoles the chief deflection may be negative in all leads, or in both Leads II and III. The third lead is, therefore, the most trustworthy for determining the side of origin, and it is fairly safe to state that upwardly directed deflections in this lead are of right ventricular origin and downwardly directed deflections are of left ventricular origin (*cf.* Fig. 100). Occasionally these premature contractions may recur regularly, giving rise to a coupled rhythm, as shown in (Fig. 148). When a premature

contraction is interpolated the waves are similar in form, but the rhythm is not disturbed by a compensatory pause.

E. Auricular Flutter (Fig. 154).—The electrocardiogram shows a continuous series of small oscillations resembling *P* waves and recurring from 230 to 350 times per minute. At intervals they are replaced by ventricular complexes, which usually have a definite relation to the auricular contraction; halving of the ventricular rhythm is very common. In other instances the ventricular complexes occur less regularly, but always in relation to an auricular wave. The *P* and *T* waves may merge or summate when the latter is prominent.

F. Auricular Fibrillation (Fig. 155).—This condition is characterized by the absence of typical *P* waves, the irregularly spaced ventricular complexes of normal contour and the substitution of finer or coarser irregular undulations or vibrations between them.

G. Paroxysmal Ventricular Tachycardia (Fig. 149).—The electrocardiogram in this condition is essentially composed of continuous series of aberrant waves, due to a series of premature ventricular systoles. The contour and direction in Lead III are determined by their origin.

H. A–V Rhythms (Fig. 145).—Several types of records may be obtained, the chief variation being the position and contour of the *P* wave. It may immediately precede *R*, in which case the *P–R* interval is greatly reduced; it may be positive or negative in direction or again it may coincide with *R* or cause a depression after its completion. All of these types of waves are characteristic whether the nodal rhythm manifests itself occasionally as a premature systole or dominates the rhythm permanently.

I. A–V Block.—In its mildest form, block of the undivided *A–V* bundle manifests itself as an increase in the *P–R* interval beyond 0.2 second. In complete block (Fig. 161) several *P* waves appear for every ventricular complex, which may be entirely normal. Prolonged conduction intervals and incomplete block may alternate in some records.

In complete *A–V* dissociation (Fig. 162) the *P* waves are regularly spaced, but without relation to ventricular complexes, and recur at fairly regular intervals. Frequently the complexes are quite normal in contour, indicating that both ventricles are excited in normal fashion; often, however, either the right or left initial complex is inverted, indicating that one ventricle is excited in advance of the other.

The complexes characteristic of complete and incomplete bundle branch block and possibly also of intraventricular arborization block have been analyzed in detail above (*cf.* page 290).

Other Changes Due to Heart Involvement.—It has already been indicated that a lengthening of the conduction time gives an early indication of the involvement of heart muscle. Aside from this

phenomenon associated with irregular heart action, certain waves appear to be related to definite pathological processes. An enlargement of the P wave is usually associated with auricular hypertrophy. In cases of mitral stenosis when such waves are often one-fifth instead of one-tenth as high as the R wave they are prolonged and often have a flattened or bifurcated top. A similar large P wave is observed when dilatation or weakening of the left ventricle occurs. Lateral displacements of the heart, such as accompany pleural or pericardial effusions, pneumothorax and lung involvements, and which also give areas of increased dulness, do not usually alter the angle of the heart; they give a normal type of electrocardiogram.

The amplitude of the R wave is, no doubt, occasionally related to the amount of current generated and, hence, to the degree of activity. That the amplitude of the R wave is, on the whole, not a reliable index of the vigor of cardiac contraction, however, is indicated by the fact that small R waves are often found in individuals who, we have every reason to believe, have strong heart action. Furthermore, extrasystoles, well-known to be weak contractions, give larger R waves than are normally found. Finally, there is some reason to think that the R wave is in no way associated with muscular contraction, at least with the contraction of those muscles which are concerned in the production of effective systoles.

The size of the T wave has, with perhaps more reason, been regarded as an index of the cardiac power. Thus, Lewis points out that a large T wave occurs in cases which possess vigorous heart action (*e. g.*, in goiter cases and in animals after asphyxia). The fact that the T wave is small after weakening influences as chloroform, poisons or hemorrhage, has led some investigators to consider a small T wave an indication that a weak action of the ventricle exists. Kraus and Nicolai stated that if this wave is negative it means in 80 per cent of cases that a dangerous condition is present. The fact (Samojloff, Lewis) that a negative wave sometimes occurs in apparently normal men and that the wave becomes inverted after the use of digitalis (Cohn) seemed to lessen its diagnostic significance. Lewis, however, points out the significant fact that a negative wave is never found normally in Leads I or II, but is common in Lead III.

A recent study of the mortality rate in individuals presenting a negative T wave, particularly in Leads I and II, indicates that the prognosis is unfavorable, provided, of course, that negativity due to digitalis is excluded (Willius) (*cf.* page 290).

Use of the Electrocardiogram to Detect Valvular Lesions.—Obviously, the electrocardiogram can give no direct evidence of the existence of valvular lesions. It has been shown, however, that hypertrophy of the left ventricle is usually associated with known cases of aortic insufficiency and arteriosclerosis, whereas right-sided hypertrophy accompanies congenital pulmonary lesions and mitral involve-

ment. By detecting the presence of these hypertrophies, the electrocardiogram may draw attention to unrecognized valvular lesions as well as confirm a diagnosis previously made by auscultation. This is very important, as it is a well-known fact that generally no presystolic murmur occurs in mitral stenosis when the auricles are fibrillating. It is also often valuable in clearing up a doubtful interpretation of murmurs. For instance, suppose a patient has a diastolic aortic murmur combined with a presystolic murmur at the apex, as is so common. The question arises whether the presystolic murmur is due to a condition described by Flint, or whether an actual mitral stenosis exists. If a right-sided hypertrophy is shown by the electrocardiogram the diagnosis of mitral stenosis can quite safely be made, whereas a predominant left-sided enlargement points to aortic insufficiency. Again, suppose a murmur is heard in the second interspace of a child's chest in which sounds are widely transmitted. It is difficult to ascertain by auscultation whether the murmur is produced in the pulmonary or aortic area. The type of hypertrophy indicated by the electrocardiogram would clinch the diagnosis (Lewis).

One of the most important services of the electrocardiogram consists in its ability to supply evidence as to the condition of the heart muscle, for it is well understood that heart failure depends as much on the condition of the cardiac muscle, brought about by the same toxic or infectious agent that is responsible for the leak, as on the dynamic changes produced by the leak itself. If, in cases of valvular disturbance, the electrocardiogram shows a normal conduction time, if the chambers react in normal sequence and the waves are of relatively normal amplitude, the cardiac muscle may be considered as practically uninjured and the prognosis is good. If, on the other hand, the conduction time is lengthened, the impulses blocked and the heart beat irregular, the efficiency of the circulation is impaired and the probability of an efficient compensation is less.

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CHAPTER XVI.

HEART SOUNDS AND MURMURS—THE PHONOCARDIOGRAM.

The Three Heart Sounds.—Since the time that the two heart sounds were first recognized by Harvey, and their use in diagnosis suggested by Laënnec, they have offered a fruitful field of investigation and study for physicists, physiologists and clinicians alike. The first sound, as is well known, is deeper in pitch and more booming in character, also of longer duration than the second, and, according to Haycraft, separated from it by a musical interval of a minor third. Recent investigation of the sounds has shown, however, that this must be an auditory delusion, and, according to Frank, such statements should be promptly deleted from current text-books. Einthoven also has pointed out the impossibility of giving the sounds a position in a musical scale, since they are composed of vibrations of irregular frequency and, therefore, belong in the same category as murmurs and "noises."

For years clinicians have recognized that in pathological conditions three sounds may be heard, due to a splitting or reduplication of the first or second sound. Only comparatively recently, however, Gibson in England and Thayer in America, independently, reported that in normal subjects a third sound can frequently be detected. This sound, though clear, is of lower pitch than the second and much softer than the first (according to Einthoven 200 times). Einthoven, Thayer and others believe its occurrence is quite frequent in young adults (65 per cent of cases, Thayer), but it is audible only at the apex and when the patient lies upon the left side. The observations of other clinicians (personal communications) and the published records of other investigators (Lewis) make it seem probable that its presence is not as common as at first supposed.

Physical Conditions Determining the Intensity and Quality of Heart Sounds in Different Auscultation Areas.—It is generally held that the first sound is caused by the composite effects of ventricular contraction and closure of the *A–V* valves; the second, by the simultaneous closure of the pulmonary and aortic semilunar valves. Owing to the physical nature of sound conduction, the two sounds are not heard with equal intensity over all portions of the thorax, however. Physically, heart sounds are vibrations of the heart walls, valves, blood columns and arteries. In accordance with physical laws, these

vibrations are transmitted best by solid contact, less well by liquids and least efficiently by gases. Other factors being equal, they are heard best where direct contact with the chest wall occurs (apex) or where the smallest air space intervenes (base). For these reasons, the vibrations produced at the mitral valve are best heard at the apex; those produced at the tricuspid valve, over the sternum at the level of the fifth costal cartilage. Similarly, vibrations arising at the pulmonary and aortic valves are best heard in the left and right second interspaces respectively. These areas of greatest intensity are referred to as *auscultation areas.* Normally, the first sound is louder over the mitral and tricuspid areas; the second sound has its greatest intensity over the pulmonary and aortic areas. Of the latter, the aortic second sound is generally the louder in early adult life. The sounds are also transmitted through the fluid in the veins and arteries to the supraclavicular spaces and may be here recorded (Figs. 69, 75 and 102). The intensity of the sounds also varies with the distance from their origin, hence, the second sound, clearly originating at the semilunar valves, is louder in the second interspaces and very soft or scarcely appreciated by the ear in the supraclavicular fossæ. Lastly, the intensity of the sounds is determined by the vibration periods and damping of the structures which transmit them. Structures in which the period of vibration corresponds closely to that of the sounds are thrown into resonant vibration and accordingly transmit them better.

Before the vibrations recognized as heart sounds are auscultated, they are transmitted to the chest wall. By the addition of its inherent or other mechanical vibrations, this may modify their frequency or pitch; or, it may change the amplitude or intensity by its resonance. That the thoracic wall has a pronounced modifying influence, however, even if we regard it as sufficiently damped to add no vibrations of its own, is probable, for its own period is probably not high enough to transmit cardiac vibrations faultlessly (Ohm). It must be borne in mind, therefore, that the vibrations recorded from the chest—even when the direct contact of the receiver is avoided—or the sounds and murmurs heard by the ear directly are not identical with the vibrations originating in the heart. To this question we will, however, return presently.

Auscultation and Intensification of Heart Sounds.—The heart sounds transmitted to the chest wall are made up of vibrations, the frequency of which lies not far above that to which the ear mechanism is incapable of responding. Owing to the fact that their amplitude is also small and the intensity thereby greatly reduced, it is in fact questionable whether some of them are audible (Einthoven). It should, of course, be recognized that auditory acuteness varies not only in different individuals, and depends upon the bodily or physical condition, but, also, that it can be improved by training. At its

best, however, the average ear is not able to distinguish fine differences in tone (Gerhartz), and when sounds recur rapidly it is not always able to give their correct temporal relations. When several types of vibrations, as those causing a sound or murmur, intermingle, the ear, according to inclination or training, tends to pick out the one and fails to hear the other (Lewis). It must, therefore, be recognized that, although long strides can be made by practice and training, the ear alone is far from being a perfect instrument.

Various attempts have been made by the invention of stethoscopes to intensify the sounds and so aid the ear in sound perception and differentiation. In the simple form of binaural stethoscope, in which a funnel-shaped or bell-shaped cup is applied tightly over the skin, a series of sound reflections occurs from the smooth walls, but the effect does not materially intensify the sound vibration. Such an instrument is simply a convenience for the auscultator, not a sound intensifier. Attempts have been made to intensify the sounds by giving the receiver a parabola shape upon the physical principle that the sound waves vibrating parallel to the axis are concentrated at the focus and so conducted without appreciable loss. Stethoscopes with such receivers have not been found satisfactory as intensifiers of heart sounds. According to Gerhartz, this is due to the physical fact that the sounds or murmurs are not transmitted parallel from their point of origin, but are deflected in passing through the blood and tissues to the point of auscultation.

The most effective method employed in increasing sound vibration consists in the use of a receiver closed by a hard rubber or mica disk, as in the phonendoscope and the Bowles stethoscope. This converts the system into a resonator and the sounds are accentuated because the air space is set in vibration. The inherent vibration of these instruments is high and, according to Ohm, they have a favorable decrement. From a physical viewpoint, therefore, their construction seems advantageous. Einthoven, Frank and Ohm, all authorities in matters pertaining to sound registration, have employed them to intensify sounds before registration. The apparatus has made an unfavorable impression among clinicians, however, partly because it often fails to pick up high tones which are perfectly evident to the ear, and partly because it does not reproduce the quality of the original sound. This is due to the fact that the amplitude of some vibrations is increased out of proportion to that of others (Gerhartz). The original vibrations of small amplitude may have their amplitude increased, while those of larger amplitude may be almost suppressed.

The heart sounds may also be intensified by an instrument combining a microphone receiver in circuit with a telephone ear-piece. The microphone-telephone apparatus works upon the well-known principle that when loose carbons or carbon granules are brought into contact with a membrane and a current passes through them,

the resistance is modified, as the contacts change with the membrane oscillations. These variations in the current affect the magnetic field in a telephone receiver, and so, by altering the attraction of the magnet for the disk, cause it to vibrate. These instruments, however, destroy all the natural qualities of heart sounds, and it is questionable whether they are reliable to determine more than the time relations of sound phenomena.

The clearness with which sounds and murmurs over the chest are heard in auscultation depends also on the application of the stethoscope bell (Sewall, Emmerson). It has been already indicated that the resonant vibrations of the chest wall add materially to their intensity. If the stethoscope is firmly pressed against the chest wall, it is damped and certain sounds and murmurs may become inaudible. This principle is more generally recognized in auscultating for fetal heart sounds than in listening over the thorax.

REGISTRATION OF HEART SOUNDS AND MURMURS.

In the registration of heart sounds it has been the endeavor to supplant the ear-drum by some mechanism which is more sensitive and, at the same time, gives a permanent and objective record of the sounds. Of the numerous devices that have been designed to accomplish this, it will be possible to describe, briefly, only those that have been found practical as well as reliable.

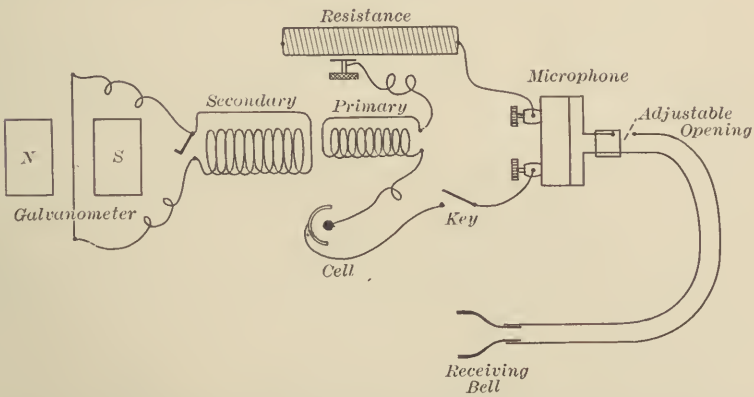

FIG. 101.—Diagram showing the arrangement of the electrocardiograph and microphone to record heart sounds by Einthoven's method.

Einthoven's Phonocardiograph.—Einthoven registered the sounds by placing a microphone in circuit with a string galvanometer. The diagram of Fig. 101 shows the principle of this apparatus. In detail, the bell of a stethoscope fastened to the chest by adhesive is connected by rubber tubing about 75 cm. long to a suspended microphone.

In the system an adjustable opening guarded by a valve is introduced. By opening the valve, to a certain degree, the system operates on the principle of the tachograph (Frank), eliminating the relatively slower oscillations of the apex, while the more frequent sound vibrations continue to be transmitted. The transfer of microphone oscillations to the string galvanometer is accomplished by placing, in circuit with the microphone and battery, a primary coil without a core and a rheostat of approximately 70 ohms' resistance. The current induced in the secondary is communicated to the galvanometer. The intensity of this current can be varied by the distance between the primary and secondary coils and also by the resistance introduced by the rheostat. The registration of the string movements occurs as described for the electrocardiogram. Instead of the string galvanometer a suitable form of oscillograph may be substituted (Watson and Wemyss).

Critique.—The sound vibrations registered by Einthoven's method are so characteristic and variable as to create the impression that they are recorded in a perfect manner. There can be no question that the string used by Einthoven had a vibration period far in excess of that necessary to accurately record heart sounds. This, however, does not follow in the case of heart sound records taken by every string galvanometer. The more serious deficiency in the method lies in the microphone system. Frank pointed out that the vibration frequency of the microphone system, which is also concerned in sound transformation, in no way equals that of the string. In addition, as Williams points out, the undamped motion of the carbon particles introduces artefacts in the transformation of sound vibrations into electrical variations. Furthermore, the transmutation of direct electrical variations into those of the secondary circuit, where changes in intensity play a predominant rôle, introduces a possible source of error in the absolute registration of sounds.

These shortcomings, however, are minimal as compared with those of other methods at present available, and hence, this procedure remains one of the best when its physical as well as its practical aspects are considered. The only practical drawbacks are the expense, the bulk of the apparatus involved and the technic required for its manipulation.[1]

Williams' Modification of the Indirect Method.—In order to overcome the difficulties incident to the use of a microphone, Williams employed an electromagnetic telephone provided with an air-damped diaphragm having a high inherent frequency. A shallow ring passed around the telephone cap served as a "mouth-piece" and a small lateral opening maintained the atmospheric pressure, except during a sudden variation due to the heart sound vibrations. This device is applied

[1] For details of technic *cf.* Battaerd, Heart, 1915, **6**, 121.

directly to the chest wall. The currents produced by the telephone are amplified by a four-stage amplifier and connected to a string galvanometer. In recording murmurs, a condenser is placed in series, and its capacity may be so chosen that the comparatively low-pitched first and second sounds are partially suppressed, while vibrations of the higher pitched murmurs are transmitted undiminished. In this way, it is possible to produce the necessary amplification of the murmur records without the enormous excursion which the first and second sounds would produce. While this apparatus should serve useful ends for research purposes, the skilful technic required, in order to eliminate adventitious "noises" and prevent the breaking of a large number of galvanometer strings, together with the need of a galvanometer of much higher inherent frequency than is generally available, do not recommend this method at present for clinical use.[1]

Direct Registration of Heart Sounds.—The direct method of heart sound registration endeavors to copy more or less the principle used by the human ear in auscultation. A funnel or stethoscope bell of appropriate size is snugly applied over a cardiac area, and the sounds led by heavy rubber tubing to a capsule covered by a very light membrane. This membrane may be compared to the tympanic membrane of the ear. The conveyed sounds cause both to vibrate; in the case of the ear, the vibrations are transmitted by a series of auditory ossicles to the internal ear, and are then transformed into nerve impulses registering in the auditory cortex; in the case of artificial membrane, the vibrations are photographed in some way on sensitive films.

In accordance with these ideas, Frank, in 1907, devised a registering capsule upon which a small lever corresponding to the head and two handles of the malleus played. By placing the levers, corresponding to the long handle, in the pathway of a projecting light system, successful heart sound records were obtained in certain cases. A similar procedure has recently been described by Hess, and, to judge from the character of the reproduced curves, forms a very efficient device for registering heart sounds. The inconvenience of using systems involving microscopic projections, and the difficulty of obtaining tracings of requisite photographic excellence (*cf.* Hess) have limited the employment of such forms of apparatus.

For these reasons, chiefly, Frank altered the construction of his apparatus so that the vibrations of a membrane could be photographed through beams of light reflected from tiny mirrors attached

[1] The audion amplifier has been employed on several occasions to reproduce the heart sounds for assemblies, and Myres (Jour. Am. Med. Assn., 1922, **78**, 100) has recently attempted to record heart sounds on the telegraphone—a form of electric phonograph. The graphic records reproduced by this investigator could not, however, be interpreted as heart sounds or murmur vibrations by the most vivid imagination.

to them. This led to the development of the segment capsule, the shape and mounting of which have already been described (Fig. 59). The capsules are covered by very thin rubber dam or, as was suggested by Weber, with mesentery from a guinea-pig. This capsule is directly connected by a piece of rubber tubing (about 70 cm. long), having an adjustable side opening, to a stethoscope bell or preferably a phonendoscope applied directly to the chest. When the side tube is closed there is recorded a large record of the apex-beat superimposed upon which are the heart sound vibrations (Fig. 102). In some respects this represents the ideal form of record, for, in this way, the time relations of the sounds to the apex-beat are directly established, and the sounds heard by a closed system represent the sum total of impact and sound oscillations. To rule out the larger oscillations, the procedure of Einthoven is made use of, namely, to partly open the

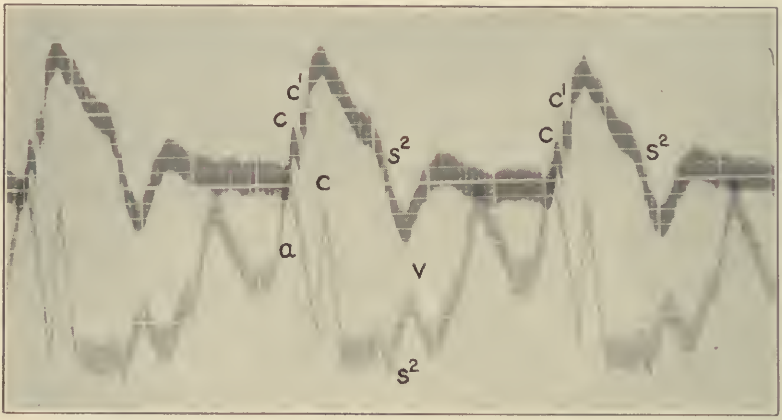

Fig. 102.—Heart sounds superimposed on apex tracing (upper) recorded simultaneously with supraclavicular venous pulse (lower); *c*, initial vibrations; c^1, valve vibrations; s^2, second sound, also shown transmitted to jugular.

system to the external air. By this procedure, records have been obtained by Frank and Hess, as well as Edens, which resemble in many details those obtained by the string galvanometer, and leave no doubt from their general character that they are true heart sounds (Fig. 79).

In 1913, Brömser and Frank described a new apparatus for recording sounds. It consists of a capsule covered with a very thin piece of isinglass, upon the most expansible part of which a tiny mirror (1 mm. diameter) is placed. Damping is secured by placing very close to the internal surface of the membrane a damping plate with a very tiny opening. The adaptability or superiority of this apparatus for recording heart sounds has still not been reported upon.

The Modified Capsules of Wiggers and Dean.—In attempting to use the Frank capsules in sound registration, it was found that a more

sensitive membrane, protected from extraneous air vibrations, was necessary in order to record the heart sounds from average adult individuals. The sound recorder, shown schematically in Fig. 103, *B*, was therefore devised and substituted in the cannon carriage for an ordinary segment capsule (Wiggers and Dean). This capsule consists essentially of a segment capsule, *d*, with an external outlet, *e*. Over the surface a delicate rubber film, *f*, is formed by passing the opening of the capsule through rubber cement and subsequently stretching the partially dry film in order to increase its tension. Before the film has completely set or dried, a tiny mirror (1 or 2 mm. square) is deposited upon it and allowed to adhere, and virtually becomes a part of the membrane. To protect this membrane from sound vibrations in the room, as well as from air currents, it is enclosed in a housing, *g*, having a front window of glass. In this housing is a conical vent, *o*, which permits equalization of pressure much as the

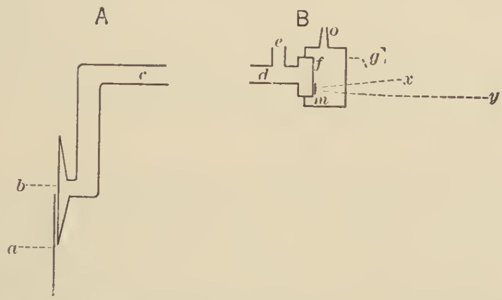

Fig. 103.—Diagram showing essential parts of sound-recording apparatus. *A*, sound receiver for direct work on heart; *B*, sound recorder connected either with apparatus shown in *A* or with stethoscope bell applied over thorax; *d*, receiving tube; *e*, adjustable side opening; *f*, delicate rubber film; *m*, reflecting mirror. Housing contains front window, *g*, and a small vent, *o*, for equalizing pressures. (After Wiggers and Dean.)

Eustachian tubes of the middle ear. In other words, the housing is regarded as corresponding to the middle ear, the membrane to the tympanic membrane and the entering tube, *d*, to the auditory canal, to which sound vibrations are led by as short a tube as possible. By means of this apparatus, satisfactory sound records may be obtained on all normal individuals, and murmurs of the louder type may be recorded in clinical cases. Such records compare favorably with those obtained by the phonocardiograph of Einthoven and the technic of their use is very much simpler.

Critique.—The vibration frequency of optical capsules themselves is sufficiently high, and their theoretical analysis has been carried out, so that they themselves are not open to criticism. The chief drawback of the original Frank capsules consists in the fact that, when the system communicates with the outside air, the use of a phonendoscope is necessary, for otherwise the capsules are not suffi-

ciently sensitive to respond to the heart sound vibrations. The use of a phonendoscope is justified by Ohm on the ground that its inherent vibration is high and it has a favorable decrement. Gerhartz, however, points out that it acts as a resonator, and so its employment is fraught with some suspicions as to its accuracy in depicting heart sounds. This criticism does not apply to the author's modification, in which the use of a phonendoscope is dispensed with and the sounds transmitted directly. Gerhartz further questions whether, by opening the communicating tube partially to the outside air, it is possible to obtain sound records that are absolutely free from mechanical vibrations. Whether or not it is possible to do this depends upon the sensitiveness of the recording membrane and the size of opening permitted in the side tube. That it is possible to obtain such records by the modified capsules is evidenced by the fact that they rise from the same base-line and oscillate to each side of this line (Fig. 64, *C*). On the other hand, there is no doubt that this cannot be accomplished when the sounds or murmurs are weak and distant or when the chest wall is even moderately thick. In order to obtain any record in these cases, it is necessary to close the side tube considerably, in which case mixtures of mechanical impacts and sound vibrations are evidently recorded (*cf.* Fig. 64, *D*).

Registration with Ohm's Gelatine Membranes.—In the apparatus devised by Ohm, the vibrations are reproduced by a gelatine film made by dipping a ring into a gelatine solution and allowing it to cool. A small mirror which reflects a band of light, as in the case of Frank's capsules, is mounted centrally on the gelatine by a narrow strip of very thin paper fastened peripherally to the ring. The damping of the membrane may be varied by slipping a chamber over the closed tube and so varying the depth of the capsule chamber. The capsule is connected by tubing with a phonendoscope, which is not directly in contact with the chest wall but mounted upon a hard wooden base 0.5 cm. in thickness. The idea is to eliminate all the coarser vibrations due to the apex-beat.

Critique.—Since the apparatus is familiar to the writer only through its description, it is difficult to give a critical analysis, especially since no details as to its parts are given. The fact that it has (according to Ohm) a vibration frequency of 200 is in its favor. The arrangement of the mirror is theoretically less desirable than that of Frank's capsule. The apparatus, as far as the writer is aware, is not in use in this country or in England.

Registration with Gerhartz's Apparatus.—In the apparatus of Gerhartz an attempt is made to prevent the cardiac impact by the use of a conical receiver closed below by a wooden diaphragm (4 mm. thick), which is perforated with very small holes. The vibrations are transmitted by rubber tubes without the employment of a phonendoscope to a collodium membrane 20 mm. in diameter. The oscillations are

transmitted by a bamboo splinter resting in a holder to a tiny steel platelet, oscillating by two needle points in holes of the magnet poles. Upon this plate a tiny mirror is fastened, and by varying the relation of the two electromagnetic poles the position of the mirror is altered. Since the electromagnet causes its return to a position determined by the lines of magnetic force, its movements are electromagnetically damped. The movements of the mirror are photographed by reflecting a band of light.

Critique.—Gerhartz gives no data as to the constants of his apparatus, nor has its inherent vibration frequency apparently been established. One would judge its period to be low, from the appliance used to communicate the membrane movements to the mirror. No details are given as to the grade of damping. Much that applies to the discussion of the apparatus of Weiss very possibly also applies to this apparatus. It has, furthermore, the serious drawback, which Gerhartz himself points out, that the oscillations are recorded in insufficient amplitude for careful study, while the records obtained are technically so poor that they cannot, as a rule, be reproduced in illustrations. Gerhartz's illustrations are, therefore, nearly all copies, in the making of which extreme care was evidently not always exercised.

Registration with Weiss's Phonoscope.—The central portion of this apparatus consists of a metal box, on one side of which is a plate containing in its center an opening. This is covered by a film of soap. The roof supports a delicate lever of silvered glass, the vertical arm of which is bent horizontally. The end of the horizontal arm terminates in a small loop, which is brought into contact with the soap film by an adjustment screw. The vibrations of the soap film are transmitted to the horizontal arm of the glass lever, and the similar movements of the vertical arm are recorded by projecting its shadow upon a photokymograph. The heart sound vibrations are transmitted to the membrane from a funnel, which is not in direct contact with the chest, but, to avoid the cardiac impact, is suspended by a holder fixed to the chest so that its free end is separated from the chest wall.

Critique.—The apparatus is evidently very sensitive and, as used by Weiss and Joachim, Bull and others, has yielded records of very respectable amplitude. Even fetal heart sounds have actually been recorded by Hofbauer and Weiss. The introduction of this instrument has given rise to the liveliest discussion, not only as to its ability to reproduce heart sounds, but also as to the principles upon which sound registering apparatus should be constructed. Inasmuch as these principles are of general application, the discussion may be briefly reviewed.

Frank, who has studied the subject most thoroughly, has emphasized the fact that the sound vibration can be accurately reproduced

only by an apparatus, the inherent vibration frequency of which exceeds that of the sound to be recorded. When this requirement is not fulfilled, the curves are distorted by friction and inertia and must be corrected by laborious procedures. When it is fulfilled, and the instrumental period is known, damping is not essential or should be present only to such a degree that the instrument is not quite aperiodic. If the damping is greater, assurance must be had that the deflection period remains less than the interval required for the smallest deviation to take place. Frank believes that the records obtained by Weiss's apparatus are nothing more than the inherent vibrations of the glass lever, which has a frequency of 22 per second. In support of this, he cites the fact that the periods of different sound vibrations are nearly the same and show only a small decrement. Weiss has replied to this that, in the first place, the period of the lever is calculated too low by Frank, and, in the second place, that this is of no great importance, since the instrument was damped more than sufficient to render it aperiodic and its deflection time was 0.01 of a second.

Hermann, pointing to the success of the phonograph, has opposed Frank's contentions that a vibration frequency in excess of that of the oscillations is necessary, provided the instrument is damped enough to render it aperiodic. According to this doctrine, it would be possible to increase the sensitiveness and obtain larger oscillations in the recording membrane through resonance by selecting a membrane the inherent frequency of which approximates that of the process to be recorded. Frank has subsequently definitely denied the physical soundness of this principle, and has pointed out that nothing is gained, as far as accuracy is concerned, by an extreme degree of damping. Furthermore, he states that an examination reveals the fact that this principle has never been successfully applied to any sound recording device, neither the phonograph nor the eardrum being modeled upon it.

We may conclude, therefore, that the most that can be hoped for from Weiss's phonoscope is that it records with approximate correctness the occurrence and time relations of the different sounds. Upon the period and amplitude of the vibrations no reliance can be placed.

A much better principle of rendering soap film vibrations visible was devised by Garten, who supported a tiny splinter of steel on a very tiny soap-bubble, centered it by a magnetic field and recorded the movements of its shadow on a photokymograph. While very useful in registering voice sounds, its practical value in registering heart sounds has not been established.

The author has seen records of human heart sounds and murmurs recorded by this apparatus in Garten's laboratory, but personal attempts to use it for this purpose have not been successful. The sensitiveness, like that of the ordinary Frank capsule, is apparently not adequate for use in the average clinical case.

NATURE AND TIME RELATIONS OF PHONOCARDIOGRAMS.

The Character of Heart Sound Tracings.—In interpreting the nature of heart sound tracings, it is important to utilize only such records as give fair assurance of technical accuracy. The sound records obtained by the phonocardiographic method in Einthoven's laboratory may be said to have set a standard with which records obtained by other methods may be compared. As illustrated in Fig. 104, they show that the vibrations start from a horizontal line and oscillate above and below it, that the duration and amplitude of the consecutive vibrations are very variable and that these characteristics change in different individuals. Most of the published tracings taken by direct methods show no similarity to these tracings. This is the case of records published by Bull, Van Zwaluwenburg and

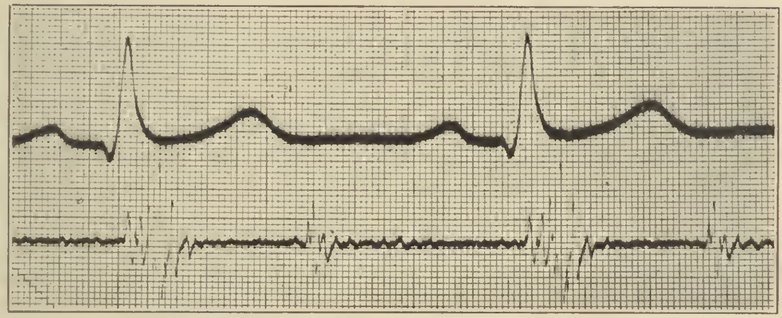

FIG. 104.—Simultaneous records of electrocardiogram and heart sounds, showing relation of latter to waves of the electrocardiogram. (Courtesy of Dr. H. B. Williams.)

Agnew, Weiss and Joachim, Gerhartz and Ohm. Records which compare more favorably with those of electrocardiographic records have been obtained by Frank on dogs and by Edens on selected patients. A record obtained from the apex region, by the direct registering capsules of Wiggers and Dean, is shown in Fig. 64, *C*, *D*, and it is obvious that it conforms with those taken by the phonocardiographic method of Einthoven. In such records, as well as in those obtained by the Einthoven method, the first sound is distinctly longer than the second, and the amplitude of vibrations is larger. Both sounds reach a maximum amplitude rapidly and after a swift decrescendo, stop abruptly.

The details of the first apex sound, as analyzed by Battaerd, may be found in a large number of tracings and are well illustrated in Fig. 105. The sound begins with a small introductory vibration, *A*, often very pronounced, again barely perceptible and not infrequently absent. The period of this vibration is much longer than that of

the second set, and it may start either as an up or a down stroke. This is followed by a variable number of waves (usually five to seven), *B*, the onset of which is also abrupt. These vibrations reach their maximum amplitude rapidly and then decline, merging into a set of *final vibrations*, *C*. Not all recorded sounds show these divisions so clearly, but, as a rule, their constituent parts are distinguishable (*cf*. Figs. 64, *C*, 79 and 104).

The second sound vibrations are fewer in number and not divisible into groups (*cf*. Figs. 104 and 105).

The two most unanticipated facts regarding the heart sounds which the phonocardiogram reveals are: (1) That they are not sounds in a musical sense, and (2) that their vibration frequency is very low. The records of Einthoven, Frank, Fahr, Lewis, Battaerd, Hess, Wiggers and Dean and others all show that in each sound vibrations of different periods and amplitudes occur, indicating that it is a mixture. As Einthoven points out, these composite vibrations are unlike in different individuals, but recur exactly from one cycle to the other in any one person.[1] Gerhartz calculated the average frequency per second from Einthoven's curves to be 39.4 for the first sound, 47.5 for the second and Einthoven gives 50 for the third. Frank and also Lewis find the average vibration frequency to be near 40 per second, although the latter observer has noted a vibration frequency of 70 per second in the first sound and one as high as 86 in the second. According to Lewis, sounds have, as a rule, a lower frequency than murmurs, which vary from 41 to 107 per second.

By enlarging the original plates upon which heart sound vibrations were inscribed, Battaerd found that many of the lines are really composed of small vibrations. These ultimate vibrations, comprising the first sound, ranged between 139 to 1000 per second. Such vibrations as are decipherable in the records obtained by the author correspond more nearly to the figures given by previous investigators: those of the first sound ranging, in my records of normal men, from 38 to 156, with an average of 45; those of the second sound from 50 to 80, with an average of 58. In a more recent analysis of direct records obtained by his own apparatus, Hess places the vibration frequency of the first sound between 53 and 103. Kanner reports a frequency of 47 for the first sound and 55 for the second sound, recorded by Ohm's apparatus.[2]

The following table indicates the average duration in seconds found by different observers for the two heart sounds recorded from the apex:

[1] This statement is not precisely correct, for the contour of the vibration groups are affected by inspiration and expiration.

[2] Other average frequencies are found in the literature, but, owing to the nature of the recording apparatus, their reliability must be questioned: Weiss, first sound, 77; second sound, 86. Gerhartz, first sound, 55; second sound, 63. Kapff, first sound, 34; second sound, 39.

	I sound.	II sound.
Einthoven	0.139	0.079
Einthoven (apex)	0.004	0.042
Kahn	0.109	0.081
Weiss	0.068	0.071
Gerhartz	0.076	0.045
Roos	0.034–0.039	0.043–0.044
Lewis	0.120–0.19	0.070–0.130
Hess	0.125–0.175	0.060–0.100
Kanner	0.16	0.10

The relative durations of the three components of the first sound have been determined by Battaerd and Hess, with the following results:

	Introductory vibrations.	Main vibrations.	End vibrations.
Battaerd	0.06	0.12	Variable
Hess	0.025–0.056	0.056–0.075	0.025–0.056

In comparing the records taken from the second intercostal space and the apex, investigators have found that the first sound is usually shorter in the first locality, and that a delay varying from 0.02 to 0.06 second usually occurs before the sound begins at the second intercostal space. Fahr suggests that this delay is due to the fact that the initial vibrations can usually not be detected in the aortic or pulmonary areas, either because the current in the microphone circuit cannot be made sufficiently intense or because they cannot be separated from certain accidental vibrations nearly always present. It is more probable, however, that the earlier vibrations are not transmitted as easily to the second intercostal space as to the apex and that the difference in time is due to the fact that the first vibrations are not recorded. In precise studies involving accurate time relations the apical sounds should therefore be used.

The time relations of the sounds to the carotid rise, the intraventricular pressure (in experimental animals) and to the waves of the electrocardiogram have been frequently investigated. The results obtained by several men are gathered into the following table:

Author.	Before carotid rise.	I sound. After rise of *R* wave, electrocard.	I sound. After rise of intraventricular pressure curve.	II sound. After carotid rise.	II sound. After end of T. electro-card.
Einthoven (man)	0.160	—	—	0.12	—
Weiss (man)	0.067 0.075	—	—	.20	—
Frank (dog)	0.059	—	—	0.106	
Gerhartz (man)	0.042 0.133	0.06	—	0.214	0.048
Kahn (man)	0.067	0.028	—	—	0.031
Wiggers (man)	0.116	—	0.00 (animals)	0.24–0.035	
Lewis (man)	..	0.022 0.026	—	—	0.028
Lewis (dog)	—	0.01–0.03	—	—	Before end.
Fahr (man)	—	0.02–0.03	—	—	0.010–0.02
Bull (man)	—	0.03–0.04	—	—	0.005–0.01
Wirth (dogs)	—	—	0.025	—	
Roos (man)	0.06–0.09	—	—	—	—

As may be anticipated, the relations of the sounds to the carotid rise are very variable. The most satisfactory method of determining this relation, and the one which is automatically corrected for conduction time, is to record them by Frank's capsules, superimposed upon the venous and arterial pulses from the supraclavicular region (Figs. 69, 75 and 102). The average of a number of such records indicates that the first sound occurs before the subclavian rise by an interval of 0.116 second, while the second sound begins from 0.015 to 0.035 second after the beginning of the incisura or beginning of diastole.

THE NATURE AND TIME RELATIONS OF THE FUNDAMENTAL HEART SOUNDS.

In studying the causes, characteristics and chronotropic relations of the sounds by recording mechanisms, it is important to have accurate records of the fundamental vibrations as they occur in the heart. It is questionable, however, whether the vibrations recorded from the thoracic wall are duplicates of the fundamental vibrations originating within the heart. There are theoretical as well as experimental reasons for believing that vibrations may be deleted or added to the fundamental vibrations before they reach the receiver placed upon the chest. As the amplitude of sound vibrations decreases directly with the distance that they are propagated, it is conceivable that vibrations of small amplitude may fail to reach the thoracic wall or become too small to be recorded. The extent to which depression occurs in the apex region depends on the volume of intervening lung, which varies not only in different subjects but, in the same individual, with the phases of respiration. In this way, Fahr and Battaerd have explained the frequent variations in contour and grouping of the first sound vibrations taken from the apex region. Owing to the greater distance between the base of the ventricles and chest wall, even larger fundamental vibrations originating in the aorta and pulmonary artery may fail to reach the thoracic wall. Consequently, sound vibrations are not only more difficult to record from the second interspaces, but are subject to even greater variation in grouping and contour.

Vibrations may be added to the fundamental vibrations in several different ways. In the first place, adventitious respiratory sounds may be incorporated with the fundamental vibrations. This may occur even during expiratory apnea, for each change in the volume and position of the ventricles exerts a cardiopneumatic effect on the lungs capable of creating sound vibrations within lung tissue. In the second place, the thoracic wall may be thrown into vibration by mechanical impacts, as is well known to be the case in thoracic percussion. Conditions for inaugurating such an inherent vibration of the chest wall are especially favorable at the onset of ventricular systole (*i. e.*, during

the first sound), owing to the fact that at this time the ventricular apex gives an impact to the thorax. How important this factor is cannot be established until the vibration frequency and decrement of the inherent thoracic vibrations are known. That it varies greatly with the type of thorax and vigor of the apex impulse must be logically conceded.

Finally, the relative amplitude of the transmitted fundamental vibrations may be altered. The heart sounds are composed of vibrations varying greatly in their individual periods. The air-containing thorax, which acts as a resonator, may, therefore, intensify the amplitude of those vibrations with which it is capable of vibrating in unison and reproduce them out of proportion to other vibrations which differ essentially from the inherent thoracic period. In these ways the configuration of the sound groups may be altered or certain waves entirely repressed.

In order to study the fundamental heart sounds as they occur in the heart, Wiggers and Dean devised a sound transmitter capable of picking up the sound vibrations from any point of the exposed heart and transmitting them to a sensitive recording capsule.

The essential features of the sound transmitter are shown in Fig. 103, *A*. This apparatus consists of a light segment capsule, 23 mm. in diameter, and covered with a very tensely stretched rubber membrane. To this is fastened a very light trapezoidal plate of aluminum continued into a rigid lever, *a*, also of aluminum. This stylus, which has an eyelet at its end, is fastened by a stitch to any portion of the heart, *e. g.*, ventricle, auricle or aorta. Several of these instruments may be applied simultaneously to the heart in this way, the only limitation in number being that contact of the different transmitters with each other or with apparatus must be avoided.

The sound transmitter is connected by soft rubber tubing, 30 cm. long, with the sound recorder apparatus shown in Fig. 103, *B*, and already described. By applying this sound receiver to various portions of the heart, it was found that two essentially different types of records were obtained in the case of the first sound, depending on whether they were attached to the ventricles or conus of the aorta or pulmonary artery. These two types of waves, illustrated in enlarged forms in Fig. 105, are designated as the ventricular and aortic sounds respectively.

The Components of the First Ventricular Sound.—The vibrations recorded from different regions of the right and left ventricle show no essential differences; hence, they may be referred to in common as the *ventricular sounds*.

The first ventricular sound of the dog is composed of a series of five to thirteen irregular vibrations, the periods of which range from 0.004 to 0.054 second. As their maximum period rarely exceeds 0.024 second, it is doubtful whether vibrations of longer period really

may be considered as entering into the sound complex. The duration of the sound varies from 0.05 to 0.152 second. The components of the first sound are clearly discernible in enlarged form in the upper record of Fig. 105. The sound starts with an *introductory vibration, A*. Occasionally there are two of these vibrations. This is followed

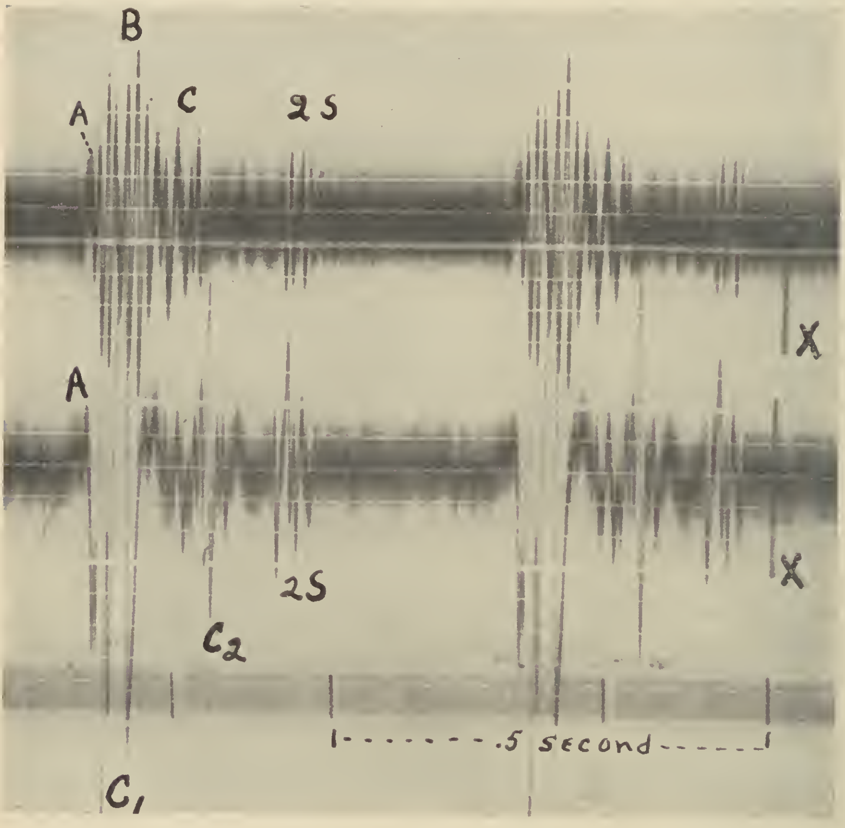

FIG. 105.—Records of ventricular sounds (upper record) and aortic sounds (lower record), enlarged three times and showing details of sound vibrations. *A*, introductory vibrations; *B*, main vibrations; *C*, final vibrations in ventricular sound record; C_1, first component of main vibrations in aortic record; C_2, second component; 2*S*, second sound.

by a group of five or six *main vibrations, B*, the onset of which is always distinctly indicated by a sharp deflection of the light band, either in an upward or downward direction. They are followed by a group of *final vibrations, C*, varying in number. In short, *the fundamental sounds taken directly from the ventricles are practically duplicates of thoracic sounds recorded from the apex.*

The Components of the First Aortic Sound.—The first sound recorded directly from the aorta or pulmonary artery, as a rule, contains more vibrations than the corresponding first ventricular sound. Its duration varies from 0.028 to 0.15 second. The aortic vibrations, like those from the ventricle, may or may not start with an *introductory variation, A*. It may be present in one record and not in the other when synchronously recorded. Hence, discrepancies occur if we attempt time comparisons between the two sounds from the first recorded introductory variation. Following the introductory variation, we recognize a group of large oscillations that will be referred to as the *first component* (labeled C_1 in Fig. 105). These oscillations start precisely with the main vibrations of the first ventricular sound. The periods of this component do not correspond vibration for vibration with the ventricular sound, nor is the maximum amplitude reached synchronously. As a rule, the frequency is greater and the maximum reached earlier in the aortic curves (Fig. 105). Following these vibrations, comes a *second component* (marked C_2 in Fig. 105), which generally reaches a second maximum amplitude during the ejection period. In some experiments, it may be dissociated from the first component, and occur as an isolated set of vibrations during mid-systole; in other words, the first sound is reduplicated. *It is obvious that these detailed characteristics are not, as a rule, transmitted accurately to the second interspaces and that, in consequence, the sounds recorded here do not correspond to those actually present at the semilunar valves.* Only rarely have they been recognized in man. Battaerd, by increasing the sensitiveness of his microphone arrangement considerably, was able to obtain a curve in which such components are definitely recognizable, and the author has obtained a single record from a thin-chested child showing similar components.

The Time Relations of the Sounds to Other Events.—The time relations of the sounds to intraventricular pressure, aortic pressure, auricular events and the second lead of the electrocardiogram are illustrated in Figs. 106, 107, 108 and 109. The following relations are established by a study of such synchronous tracings in the case of the first ventricular sounds:

1. The two *introductory vibrations* begin during auricular relaxation (Fig. 109), precede by a variable interval the onset of intraventricular pressure (Fig. 107), and occur during the rise of the R_{II} deflection of the electrocardiogram (Fig. 106).

2. The *main vibrations,* composed of seven to thirteen vibrations of irregular period and amplitude, begin precisely with the onset of the pressure rise within the ventricle (Fig. 107), reach their maximum during the isometric period and begin on the descending limb of the R_{II} wave of the electrocardiogram (Fig. 106).

3. The *final vibrations* occur during the period when the injection of blood from the ventricle takes place (Fig. 108) and during the R–T interval of the electrocardiogram (Fig. 106).

The following time relations of the first aortic sounds are likewise established:

1. The *introductory vibrations*, comparable to similar vibrations in the first ventricular sound, occur before the elevation of intraventricular pressure, but after the end of auricular systole.

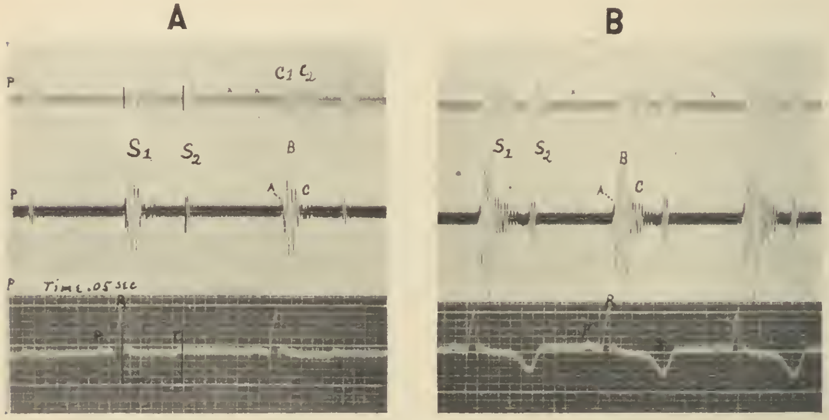

FIG. 106.—Two segments of a record showing aortic sounds (upper curve), right ventricular sounds (middle curve) and their relation to the electrocardiogram, Lead II. *A*, during hypodynamic heart action consequent to opening chest. *B*, during action of adrenalin. (One-half actual size.) *P*, alignment of points; *x*, accidental vibrations; S_1, first sound; S_2, second sound; *A*, introductory vibrations; *B*, main vibrations; *C*, final vibrations of ventricular first sound; C_1, first component; C_2, second component of first aortic sound. Ink lines show synchronous points on three curves. (After Wiggers and Dean.)

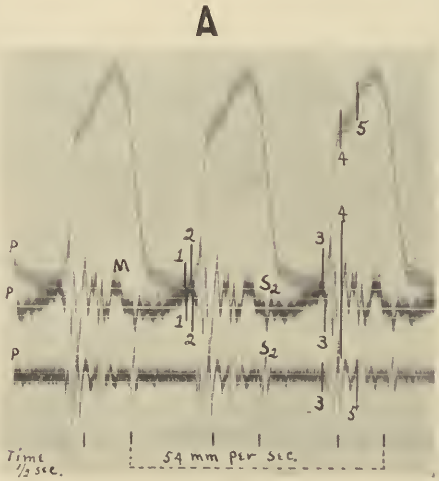

FIG. 107.—Time relation of ventricular heart sounds (middle curve) and aortic sounds (lower curve) to left intraventricular pressure (upper curve). Numerals 1, 2, 3, 4, etc., show corresponding points corrected for parallax. S_2, second heart sound; *M*, mechanical oscillation. (After Wiggers and Dean.)

2. The *first component* of main vibrations, consisting of a group of vibrations which begin synchronously with the main vibrations of the first ventricular sound, reach their maximum during the isometric period of ventricular systole (Fig. 107), and fall on the descending limb of R_{II} (Fig. 106).

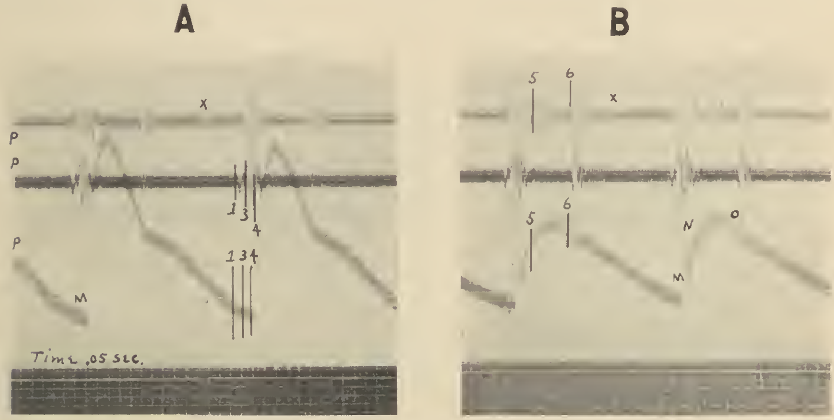

FIG. 108.—Two segments of a record showing time relations of different components of the aortic sounds (upper curve) and right ventricular sounds (middle curve) to intra-aortic pressure (lower curve). (One-half actual size.) *A*, during normal cardiac action; *B*, after compression of aorta; other numerals and letters same as before; *M*, preliminary vibration; *N*, primary oscillation; *O*, incisura of aortic curve. (After Wiggers and Dean.)

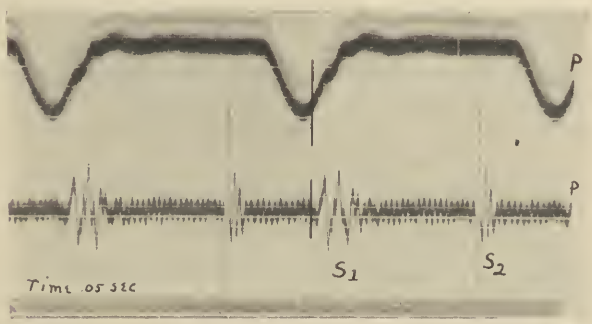

FIG. 109.—Segment of record showing relation of first right ventricular sound, S_1, to end of auricular systole, as indicated by apex of auricular myogram (upper curve). Second sound, S_2, accentuated. (About three-fourths actual size.) (After Wiggers and Dean.)

3. The *second component* of main vibrations, occasionally consecutive to the first component but more often dissociated from it so as to give the sound a reduplicated character, occurs during the ejection period of the ventricle (Figs. 107 and 108) and reaches a maximum amplitude during a variable portion of this period.

The second sounds from both the arteries and ventricles consist of a short, simple series of vibrations occurring precisely at the onset of diastole, as evidenced by their occurrence at the beginning of the diastolic fall of intraventricular pressure (Fig. 107) and the onset of the aortic incisura (Fig. 108). They precede the opening of the *A–V* valves by a considerable interval, as evidenced by their com-

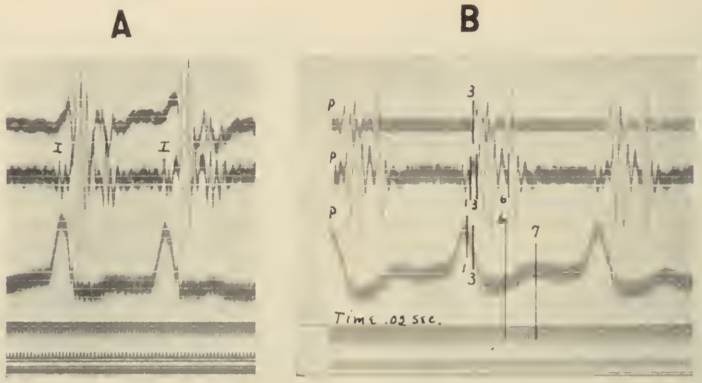

FIG. 110.—Two segments of records showing the time relations of the pulmonary sounds (upper curve) and aortic sounds (middle curve) to the right intra-auricular pressure. (One-half actual size.) Letters and numerals same as before; 7, diastolic fall of intra-auricular pressure following opening of tricuspid valve. *A*, normal; *B*, during depressed cardiac action due to pituitrin. (After Wiggers and Dean.)

parisons with the diastolic fall of pressure in the auricle (Fig. 110). They may, but do not necessarily, coincide with the end of the T_{II} wave of the electrocardiogram. The second aortic and pulmonary sounds differ from the synchronously recorded second ventricular sounds by their larger amplitude and sometimes by the greater number of vibrations.

THE CAUSE OF THE HEART SOUNDS.

Graphic records of heart sounds in animals and man leave no doubt that the main crescendo vibrations of both the apex and aortic sounds, which are probably responsible for the sound impression in auscultation, occur early in systole—in fact, during the isometric phases of ventricular contraction. This must mean that these vibrations can only be due to events which occur during this phase of ventricular systole. In 1810, Wollaston showed that the contraction of the skeletal muscle causes sound vibrations and, in 1836, a committee appointed by the British Medical Association concluded that such vibrations of muscle contraction are, in part, responsible for the first sound. In 1869, Ludwig and Dogiel demonstrated that the

contraction of the excised heart, quite independently of valve action, could cause a definite sound. In spite of these apparently conclusive demonstrations, objections have from time to time arisen. Thus, the question as to whether the muscular contraction *per se* is really concerned in its production has had its opponents (*cf.*, *e. g.*, Pezzi, Quain, etc.). It has been pointed out that the heart muscle does not give a tetanic contraction and is, therefore, incapable of producing a sound; that the experiments of Ludwig and Dogiel and others of a similar nature are fallacious, since the sound recorded may have been produced in some cases by the friction of the heart with the fluid in which it is suspended, in other cases by its direct frictional effect upon the stethoscope (Quain). To test this question further, Dean and the writer perfused portions of a cat's ventricle and by electrical stimulation caused these strips to contract rhythmically under tension. By attaching the sound receiver, shown in Fig. 102, *A*, and leading this to a microphone system and string galvanometer, we satisfied ourselves that each ventricular contraction so induced gives a series of irregular vibrations similar to the first heart sound (unpublished experiments). Similar records have been recently published by Hess. There remains little doubt, therefore, that muscular contraction *per se* is capable of producing sound vibrations.

In addition to the muscle sounds, other elements no doubt enter into the production of the first sound. Thus, it has been repeatedly demonstrated (Bayer, Giese, Gad) that closure of the *A–V* valves in a dead heart is capable of causing sound vibrations. It is generally accepted, therefore, that the first sound is fundamentally due to vibrations arising from: (*a*) The friction of the interlacing bands of contracting ventricular muscle, and (*b*) the closure of the *A–V* valves.

It is obvious, however, that such an explanation accounts only for the main crescendo vibrations and leaves out of consideration both the introductory and final vibrations of the apex sound and does not interpret the second components of the aortic sound.

Numerous investigators have attempted to show that an auricular element also enters into the first sound, and the earlier attempts at recording sounds (Krehl, Hürthle, Weiss, Roos) appeared to indicate that the first sound begins from 0.04 to 0.14 second before ventricular systole. The idea that auricular contraction or the inflow of blood occurring during its contraction is added to the first sound, therefore, received apparent support. Subsequent and more accurate studies (Battaerd, Wiggers and Dean) have shown, however, that the introductory vibrations of the normal sound begin before the onset of ventricular contraction and after the end of auricular systole, and can, therefore, not be attributed to its contraction (Figs. 107 and 109). Furthermore, when vibrations due to auricular systole *do* occur as abnormal phenomena, they precede ventricular systole by a much longer interval (*cf.* Fig. 166). There is, therefore, no good experi-

mental evidence to indicate that auricular contraction or phenomena associated with it enter into the composition of the normal first heart sound. Neither is there evidence that the papillary muscles have begun to contract as early as the introductory vibrations appear. The idea that the introductory vibrations may be due to a presystolic closure of the *A–V* valves is also not very probable, for the valves float toward a position of closure in the middle of auricular systole (*i. e.*, at the end of the dynamic phase), or much earlier than the time when these vibrations occur. Furthermore, the best evidence indicates that their closure is incomplete at this time and unaccompanied by sound vibrations. The cause of the slow and small introductory vibration (if, indeed, it may be considered as a sound vibration) has not received a logical and satisfactory explanation.

While the interpretation so far advanced accounts for the mixed character of the vibrations, it does not explain the crescendo and decrescendo grouping of the ventricular and apex sounds, nor does it explain the second component found over the aortic and pulmonary valve. The author ventures the following interpretation, which is, as far as known to him, in accord with facts. When the ventricle begins its contraction, its position changes slightly. This may produce the first feeble vibrations of the first sound. As soon as the ventricular pressure is raised to an equivalent of a few millimeters of mercury, the *A–V* valves close synchronously. Immediately following this closure, and during the isometric period, when all valves are closed, vibrations from their closure are set up within the ventricle. They are added to by the vibrations of muscular contraction, by movements of the chordæ tendinæa and by the vibrations created when the tension is suddenly directed against the semilunar valves. The vibrations from those different sources which have different periods intermingle and increase in intensity until the end of the isometric period. They are transmitted to the entire heart and through the semilunar valves to the aorta. When the period of rising tension ceases and blood is suddenly ejected, the oscillations decrease in amplitude within the ventricle, for the physical conditions are no longer suitable for maintaining vibrations. At the same time (*i. e.*, during early ejection), other conditions are created at the semilunar orifices—the blood is shot out through partially opened valves with increasing velocity and thus sets them into vibration, causing the second component of the aortic heart sounds. As the vigor of ejection diminishes in mid-systole, their intensity likewise diminishes.

When ventricular contraction ceases and the pressure within the aorta and ventricle quickly falls, it results in closure of the semilunar valves. The after-vibrations of the closed valves, together with those of the arterial column, cause the second sound. These oscillations rapidly decrease in amplitude and continue only for a short interval, because they are damped by the friction of the blood, and, as the pressure falls, their vibration frequency tends to become less.

The third sound (Fig. 117), which by registration is shown to come 0.13 second after the beginning of the second,[1] consists of vibrations of a more constant character. Gibson and Thayer think that they discovered this sound in association with a wave (*b* wave, *h* wave) in the venous pulse, and have accordingly attributed it to vibrations of the valves when they are floated into position by the inrushing blood. Direct experimental evidence is opposed to the assumption that the valves float into apposition at this time (Dean) (*cf.* page 79). Furthermore, Einthoven failed to find such waves in the subjects from whom he recorded a definite third sound. In a case reported by Lewis, this sound occurred 0.18 second after the second sound, and as it occurred during auricular systole, it could not have been due to the cause assigned by Gibson and Thayer. Gibson and Ewald have suggested that it is due to a systole of the auricle and resembles in cause the presystolic murmur of mitral stenosis. Neither the nature of the vibrations nor the time of the occurrence of the sound,[2] however, favors this etiology. The possibility that it is due to the closure at unequal times of the pulmonary and aortic semilunars is discouraged by Einthoven on the ground that the interval between the aortic and pulmonary second sound is not great enough to account for this variation. Einthoven would, therefore, regard it as due to after-vibrations of the aortic valves, the transmission of which to the apex was interrupted. As reasons for this view, Einthoven states: (1) That the duration of the second aortic tone = 0.18 second, of the second apex tone plus the third tone = 0.16 second; and (2) that the vibration frequency corresponds to the last vibration of the second pulmonic tone. With these varied opinions the cause of the third sound must be held *sub judice.*

THE CLINICAL VALUE OF SOUND REGISTRATION.

Without doubt the energetic efforts made to record the heart sounds and murmurs were in large part prompted by the hope that, by their use, unrecognizable or feeble murmurs would be reproduced with undoubted clarity or that the qualities of sounds and murmurs could be more satisfactorily determined. In these respects heart-sound records have, as yet, not equaled the trained human ear. Clinically they aid in determining the exact time relations of events in the cardiac cycle. The interval between the two sounds offers an exact estimate of the duration of the entire systole and makes possible

[1] More correctly stated, this is the average interval given by Einthoven. Actually, there is great variation in different individuals. Thus, in Fig. 111, the interval is approximately 0.16 second; in Fig. 117, at least 0.32 second. Hess reports an interval of 0.26 second; Bridgman, variations from 0.13 to 0.18 second. Tracings of Lewis show considerable differences in the time interval.

[2] *Cf.* Fig. 111.

a study of the factors modifying systole length. They enable us to distinguish between sounds of premature contraction and reduplication. They permit us to determine accurately the precise position of murmurs which are difficult to place with the unaided ear, especially when the heart rate is rapid or the rhythm irregular. The relative intensity of the different sounds may be compared with any given record. According to Einthoven, this may be accomplished by use of the formula $I = (N\,A)^2$, where N is the frequency and A the average amplitude. Thus, suppose the amplitude of sound a averages 14 mm. and that of sound b, 2 mm.; further, suppose that the vibration frequency of a averages 80 and that of b, 40. Then $a:b = (14 \times 80)^2 : (2 \times 40)^2$ or $(7 \times 2)^2 : (1 \times 1)^2 = 196$. In other words, sound a is 196 times as loud as sound b.

Factors Determining the Relative Intensity of the Heart Sounds in Different Auscultation Areas.—It is commonly accepted as a fact that the absolute and relative intensities of the two heart sounds not only offer valuable information concerning the dynamic state of the heart muscle, but also serve as a criterion of the pressure conditions in the greater and lesser circuits. This conception, based on plausible physical assumptions and fortified by clinical experience, has, however, received only cursory attention from experimental investigators.

Lewis, in his experimental studies of the recorded heart sounds, tested the effect of raising the arterial pressure by aortic compression, but was unable to corroborate the prevalent idea that high arterial pressure, *per se*, is responsible for an accentuation of the aortic second sound. On the other hand, the earlier experiments of Dean and the author indicated that the intensity of the sounds directly recorded from the heart is determined by the dynamic conditions of the circulation. Thus, we found that the vibrations comprising both the first and second sounds increased, not only in amplitude, but also in number of vibrations, when the ventricles increased in vigor and the blood-pressure was simultaneously elevated either by the injection of epinephrin, by aortic compression or by asphyxia (Fig. 108). These experiments did not determine, of course, whether the increased ventricular activity or the simultaneous increase in arterial pressure was fundamentally responsible for the accentuated sounds; nor was the question of changes in the relative intensity of sounds over different cardiac areas investigated. This unsatisfactory condition of the subject prompted the author to make a searching inquiry into the significance of accentuated and enfeebled heart sounds. The heart sounds over the apex region and the aortic and pulmonary areas were recorded simultaneously or in pairs by the direct sound recording capsules. Changes in the intensity of any heart sound over a particular area were determined by comparing the amplitude and number of vibrations entering into that sound complex before and

after modified conditions of the circulation were experimentally produced.

The effects of cardiac slowing, increased peripheral resistance, resulting in higher arterial pressure, and changes in the volume of blood discharged during each contraction were experimentally studied. The following table gives, first, a summary of the effects of these procedures on the heart and circulation, in a second series of columns, the anticipated results on the first and second sounds in different areas, assuming that the intensity of the first sound is governed by the vigor of ventricular contraction and that of the second sound by the height of arterial pressure. In the third series of columns of this table are indicated actually observed effects.

Experimental variable.	Circulatory effects.			Anticipated effects.				Observed effects.			
	Systolic discharge.	Pulmonary pressure.	Systemic pressure.	Pulmonary first sound.	Apex first sound.	Pulmonary second sound	Aortic second sound.	Pulmonary first sound.	Apex first sound.	Pulmonary second sound.	Aortic second sound.
Cardiac slowing	+	−	−	+	+	−	−	−	−	−	−
Cardiac acceleration	−	+	+	−	−	+	+	+	+	+	+
Increased arterial resistance	0	sl. + or 0	++	0	0	sl + or 0	+	+	+ +	0 or sl +	++
Increased systolic discharge	+	+	+	+	+	+	+	++	+	++	+
Epinephrin	+	+	++	++	++	++	++	++	++	++	++
Pituitrin	−	−	+	−	−	−	+	−	+	−	+

A rapid survey of this table leads to the following observations:

1. When the heart slows, the amplitude of contraction and volume of systolic discharge increases, while the pressures in both pulmonary and systemic circuit fall. On *a priori* grounds, we might expect an accentuation of the first sound in all areas but an enfeebled second aortic and pulmonic sound. Actual observation showed, however, that the first sound is reduced rather than increased in intensity.

2. Increasing the total resistance in the systemic circuit, and thereby elevating the arterial pressure markedly, causes a slight elevation of pulmonic arterial pressure but no change in the systolic discharge. Consequently, on *a priori* grounds we might expect that the first sound remains unaltered, but that both the second aortic and pulmonic sounds become augmented, the aortic more than the pulmonic. Actual experiments (*cf.* Fig. 108), however, showed also a great accentuation of the first sound both over the valvular areas and at the apex.

3. Increasing the systolic discharge and work of the ventricles,

as by rapid saline infusion, causes an elevation of pulmonary arterial pressures and a considerable increase in pressure in the systemic circuit. Consequently, we should expect all sounds to increase in intensity, which proved to be the case.

It is obvious from these results that the intensity of the first sound is not related to the volume of blood discharged by the ventricles, *e. g.*, during slowing of the heart; when the systolic discharge is increased, the first sound is reduced in intensity. Further analysis indicated, however, that the sound intensity varies directly as the systolic tension developed within the ventricles—and there is good reason to believe, with the tension developed during the isometric period of systole.

The relative intensity of the first sounds may, therefore, be safely used as a clinical index of the vigor with which the ventricular contraction is carried out.

The intensity of the second aortic and pulmonic sound varies roughly with the mean pressures in the respective circuits, but dynamic studies show that they are more definitely related to *the actual pressures existing in the large vessels at the very beginning of diastole, i. e., at the moment when the semilunar valves close.* When the pressures at the beginning of diastole increase, particularly in one circuit and relatively little in the other, an accentuation occurs, especially in the sounds referred to the circuit in which the changes predominate. This is the effect of epinephrin, as shown in Fig. 106. In circulatory conditions, in which the pressures at the beginning vary in opposite directions in the greater and lesser circuits, the intensity of the pulmonary and aortic sounds changes in opposite directions. This is well shown as an effect of pituitary extract, which causes an increase in pressure within the systemic but a decline of pressure in the pulmonary circuit at the beginning of diastole (*cf.* Table). The pulmonary second sound, as graphic records show (Fig. 110), is reduced in intensity, while the aortic second sound is accentuated.[1] Such observations are of further interest in that direct experimental evidence supplements the anatomical basis for believing that sounds heard over the second left intercostal space are transmitted from the right heart and lesser circuit, while those heard over the right second intercostal space and apex have their origin in the left heart and greater circulation.

Summarizing the experimental evidence, it may be said that, when reserve and caution are exercised, a change in the intensity of the first sound over an area is good evidence of a change in tension developed during systole of the ventricles, while a change in the intensity of the second sound over the aortic and pulmonary areas may safely be used as an index of a change of pressure at the beginning of diastole in the greater and lesser circuits respectively.

[1] For still better illustrations of these effects, *cf.* Wiggers (Arch. Int. Med., 1919, **24**, 471.)

The Character, Cause and Clinical Significance of Abnormal Sounds and Murmurs.—While the existence of abnormalities in the heart sounds or the presence of murmurs are in themselves not pathognomonic of definite cardiac lesions or myocardial derangements, they are, when taken in conjunction with other signs, a most important adjunct in diagnosis. The cause of abnormalities of the heart sounds and murmurs as well as their clinical significance has been established by three essential methods, viz.: (1) The correlation in extensive clinical experience of definite variations and types of murmurs with the subsequent history of the patient and postmortem findings; (2) the study of classification and interpretation of variations found in large numbers of apparently healthy men (for this purpose the examination of recruits for military service during the World War has presented an opportunity never equaled in scale nor understanding); (3) the correlation of abnormalities heard with their graphic pictures as shown in phonocardiograms.

Reduplicated Sounds.—When a doubling of either heart sound occurs, either the events responsible for each sound do not occur simultaneously or factors are added which result in vibrations that the ear can recognize as sounds. A doubling of the first sound at the apex occurs: (*a*) In apparently healthy individuals, and (*b*) in a variety of pathological conditions, in all of which added groups of vibrations, which precede the main group of vibrations, give rise to duplicated effects. Phonocardiograms published by Lewis, Bridgman and others indicate that these vibrations are caused by auricular activity (Fig. 166). Auricular contraction in some way, as yet not clearly understood, produces such audible sound waves: (*a*) When the *As–Vs* interval is unusually long, as in impeded *A–V* conduction; (*b*) when auricular contraction occurs without succeeding ventricular systoles, as in heart-block; (*c*) when auricular contraction is excessively vigorous, *e. g.*, in hypertrophy or plethora. In all of these instances the second element of the first sound is louder, as shown by sound records (Fig. 166). Doubling of the first sound has long been considered characteristic of asynchronous contraction of the two ventricles, but that this is an infrequent cause is now established, since asynchronous action is only observed with bundle-branch block. In such instances reduplication has been reported. Experimentally, the apex sounds are, however, duplicated neither in branch block nor one-sided extrasystoles, as far as the writer has been able to determine.

Reduplication of the second sound has been frequently assigned to asynchronous closure of the two sets of semilunar valves. Experimental evidence indicates, however, that any possible difference that is likely to occur would give only a single and, perhaps, prolonged second sound. Most of the instances heard and graphically recorded indicated that the added element is probably due to the

same cause which produces the third heart sound. In other words, the second element is in reality an accentuated third sound (Fig. 111).

When three sounds occur, they often simulate the tempo of a galloping horse, hence the term "gallop rhythm." It is obvious that such a gallop rhythm may be of two varieties: (*a*) That in which a presystolic group of vibrations are added (Fig. 166), and (*b*) that in which an early diastolic group follows the second sound (Fig. 111). Graphic records clearly differentiate these types, which are obviously of quite different importance, but this is by no means easily accomplished in auscultation, especially when the heart rate is rapid.

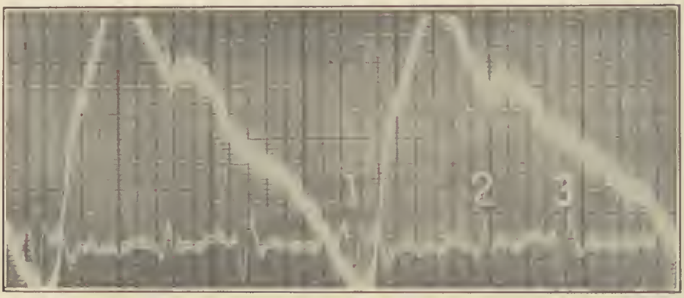

FIG. 111.—Optically recorded subclavian pulse and heart sounds by apparatus of Wiggers and Dean, showing loud third heart sound ("gallop rhythm"). Abscissæ, 0.04 second.

Cause and Character of Heart Murmurs.—Heart murmurs, like heart sounds, are composed of irregular sets of vibrations arising when the valve segments, or chordæ tendinæa, and possibly other structures within the heart, are set into vibration (*e. g.*, the walls of the aorta). By no means, all of the conditions that can possibly give rise to such vibrations are as yet recognized, not to say understood. It has long been recognized, however, that the rushing of blood through narrowed orifices sets the vibrant structures into vibrations which result in murmurs. Consequently, whenever blood enters the ventricle through narrowed *A–V* orifices or is expelled through narrowed semilunar valves (stenosis), a murmur results. Similarly, whenever blood rushes back either through incompletely closed *A–V* or aortic valves (insufficiency), a murmur is likewise produced. Recognition of these physical principles has led clinicians of the past generation universally to regard murmurs as pathognomonic signs of such valvular abnormalities. There are, however, many conditions—as both experimental studies and postmortem evidences attest—during which structures within or around the heart may be set into vibration and produce murmurs. These are termed *accidental* or *functional murmurs*.

The quality and pitch of murmurs is fundamentally governed by the character of the vibrating structures. Experience has taught that murmurs due to the vibration of stenotic valves, as a rule, have a rougher quality, while those due to leakage have a more blowing and often a more musical quality. So, also, murmurs at the aortic valves have a lower vibration frequency than those originating at the mitral valves, and are, therefore, of higher pitch. The loudness of murmurs is determined fundamentally by the velocity of movement of the blood current. Owing to this fact, faint murmurs may often be increased by augmenting the velocity of blood movement over the surfaces, *e. g.*, by increasing the venous return and consequently the systolic discharge. For this reason, murmurs frequently become more distinct after exercise, and probably this is also the reason why they are brought out by the use of amyl nitrite. Furthermore, the loudness of murmurs is governed by the same physical factors as are concerned in the transmission of heart sounds (*cf.* page 298). Consequently, murmurs are usually heard most distinctly over the corresponding valvular areas. Because of this, also, changes in position of the body as well as the respiratory position of the thorax may alter the proximity of the heart to the chest wall and determine the intensity of murmurs. Thus, murmurs of mitral stenosis are said to be heard best after exercise and when the subject lies on the left side, while murmurs of aortic regurgitation are best heard in the erect position during forced expiration, though they too are intensified by exercise (Pardee).

Systolic Murmurs.—Systolic murmurs may be due to structural defects of the mitral valves (insufficiency) or at the aortic orifice (stenosis), but they may also be present when valve action is entirely normal. The latter, or functional, systolic murmurs are more frequent than was formerly supposed. Systolic murmurs occurring at the base of the heart are usually of this type and rarely due to aortic stenosis, which is a comparatively rare lesion (Osler, Connor). The functional murmurs are usually soft and more frequently located over the pulmonic area, although they may occur over the aortic area as well. They are especially frequent in children, in anemic and in otherwise debilitated patients. They are intensified by increased cardiac action, as after exercise or during fever. It has been suggested that extracardial pressure on the aorta by normal anatomical structures are responsible for such murmurs, for a similar murmur may be produced by the application of slight pressure of a stethoscope over the exposed aorta of a dog's heart (Thayer and Macallum). Reduction in the viscosity of blood, as in anemia, likewise seems capable of setting the valves, especially the pulmonary, into vibration. Attention has already been called to the duplicated sound found normally in many animals in the aorta. Occasionally this duplication is replaced by more irregular sets of vibrations, giving the impres-

sion of a murmur. It is probable, therefore, that as blood is being ejected and the semilunar valves are approximated by blood filling the sinuses of Valsalva, the physiological conditions for the production of a functional basal murmur are always present in the normal heart. It requires only slight modification in the vigor of ejection, in the elasticity coefficient of the aorta or in the viscosity of the blood to increase their intensity sufficiently so that they become audible. Furthermore, there is more than a suspicion that the apparent disappearance of many functional murmurs occurring in young children is due to an increase in the size of the thorax so that vibrations occurring during systolic ejection are less readily transmitted, and hence no longer audible or recordable.

The basal systolic murmurs of aortic stenosis are usually low-pitched, rumbling and loud, and the intensity is greatest in the aortic area. Occasionally they may, however, be musical or accompanied by a thrill. A graphic record of such a murmur is shown in Fig. 181. The first sound is clear in its onset and the murmur does not begin until ejection has started. Weiss and Joachim believe that this differentiates these murmurs, due to aortic stenosis from those of mitral insufficiency, a conclusion that is not confirmed by records seen by the author (*cf.* also Fig. 112).

Systolic murmurs occurring at the apex are usually soft and blowing in character. Connor states that nine-tenths of the apical systolic murmurs in young adults are probably accidental or functional. The characteristics and differential features of these murmurs are that they are inconstant, disappear during rest and are increased after exercise and excitement. Furthermore, there is no tendency for them to be transmitted to the left of the apex, and they rarely have the high-pitched or blowing characteristics of those due to mitral insufficiency. Unless apical systolic murmurs are accompanied by other evidence of valvular leakage (*cf.* page 576) and a history of rheumatic infection, it is now commonly regarded as precarious to base a diagnosis of mitral regurgitation upon them.

The soft, relatively high-pitched systolic murmurs, even when obviously due to mitral insufficiency, are generally difficult to record; indeed, it is questionable whether their true character can be accurately reproduced by existing forms of apparatus (Williams). Such records are, therefore, chiefly of value as indicating precise time relations. The first-sound vibrations, as a rule, are present, but the character of the vibrations is no longer normal (Fig. 115); in other words, the murmur does not replace but follows the first sound. The murmur vibrations usually extend almost throughout systole, but not quite up to the second sound vibration. This does not indicate, however, that regurgitation fails to continue throughout systole; indeed, experimental evidence indicates that it lasts into early diastole (*cf.* page 537). Occasionally, murmur vibrations occur only

in mid-systole and are distinctly separated from the first sound (Fig. 177). The murmur vibrations are said to range from 112 to 140 per second (Lewis), but the probabilities are that they actually have a much higher frequency.

Diastolic Murmurs.—Murmurs occurring during diastole—whether proto-, mid- or late diastolic—whether present or loudest at base or apex—are practically always indicative of valvular lesions. The interpretation becomes the more certain if both systolic and diastolic murmurs are present. A diastolic murmur best heard over the aortic area, or more often over the middle of the sternum at the level of the third rib, is quite diagnostic of aortic insufficiency. In fact, the tendency is to miss cases rather than to diagnose cases too frequently (Connor). Occasionally, this murmur is heard best at the apex and, whether heard here or not, can unfailingly be recorded from this region. As a rule, it is a high-pitched, blowing murmur

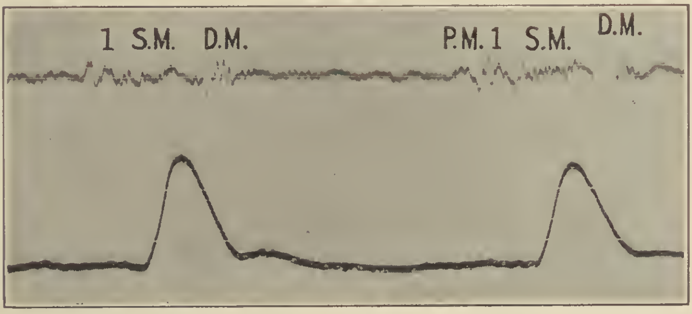

FIG. 112.—Phonocardiogram by direct method (upper curve) and radial sphygmogram from a case of aortic regurgitation. Phonocardiogram shows systolic murmur, *S.M.*, and diastolic murmur, *D.M.*, replacing second sound. Radial sphygmogram shows collapsing pulse.

but may be loud and whistling or even musical. Rarely it reaches sufficient intensity to be felt as a thrill. Phonocardiograms of these murmurs are of two kinds. The murmur may consist of a short, early diastolic vibration replacing the second sound, in which case it is diminuendo in character, and, according to Lewis, the vibration frequency is about 80 per second. Often this murmur may be so loud that the vibrations exceed in amplitude those of the first sound (Fig. 112). A systolic murmur, possibly due to associated aortic stenosis, also is usually present. In the musical murmurs illustrated in Fig. 113, the vibrations which are more like tuning-fork waves, may extend throughout diastole.

Diastolic murmurs associated with severe cases of mitral stenosis are usually best heard over the mitral area or at the apex. The presence of a diastolic murmur depends upon the grade of stenosis and upon the auricular pressure, both of which determine the rate

of inflow and extent of ventricular filling before the auricle contracts (*cf.* details of ventricular filling, normally and in stenosis, pages 95 and 545). It is said that the milder the grade of stenosis the earlier in diastole the murmur begins and the earlier it is terminated. As the venous pressure increases considerably when auricular fibrillation supervenes, the diastolic murmurs are intensified; indeed, it is often

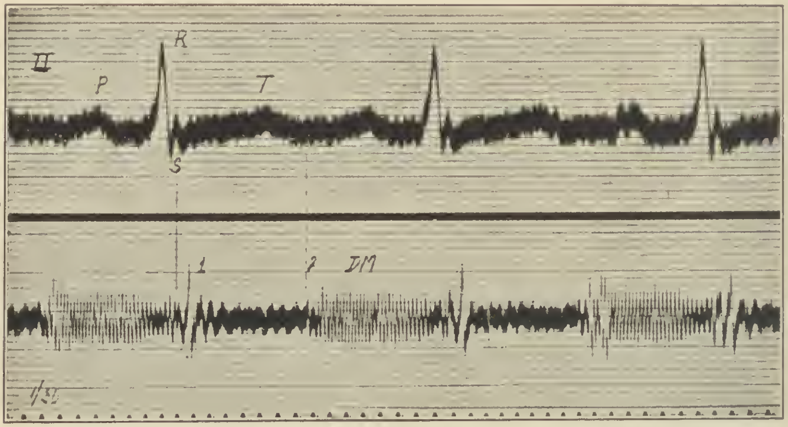

Fig. 113.—Simultaneous electrocardiogram and phonocardiogram of a musical aortic murmur. (After Lewis.)

held among clinicians that early and mid-diastolic murmurs do not occur as long as the auricles are contracting. Phonocardiograms indicate, however, that this is incorrect, at least in marked cases where diastolic murmurs may last even throughout diastole (Fig. 114). Except for respiratory variations, the murmurs are fairly

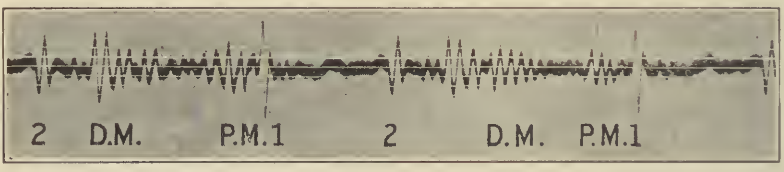

Fig. 114.—Phonocardiogram (direct method) from a case with mitral lesions, showing, in addition to first and second sounds, 1, 2, a presystolic murmur, *P.M.*, and a long diastolic murmur, *D.M.*, beginning a short interval after the second sound.

constant in character. Usually they reach their greatest intensity about 0.07 to 0.09 second after the second sound, *i. e.*, during the rapid inflow phase, and then shade off gradually until the onset of auricular systole, when a presystolic murmur supervenes (Fig. 114). During fibrillation the murmur is much intensified and varies greatly from beat to beat (Fig. 115).

Often a diastolic murmur may also be heard in cases of mitral stenosis over the pulmonary area (Graham-Steell murmur), which is quite generally attributed to relative incompetence of the pulmonary semilunar valves. Graphic studies of this murmur have apparently not been made.

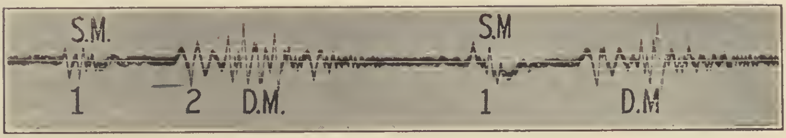

FIG. 115.—Phonocardiogram from a case of mitral lesions, showing, in addition to abnormal first and second sounds, a short systolic murmur replacing the first sound, *S.M.*, and a diastolic murmur varying in length and character from cycle to cycle.

In double lesions of the mitral valve—a frequent fact—systolic and diastolic murmurs may both appear; occasionally, they may merge, thereby obliterating entirely the first sound. (*cf.* Wiggers.)

Presystolic Murmurs.—Murmurs occurring at the very end of diastole and just before ventricular systole are designated as *presystolic*. Usually they occur during auricular systole and might, therefore, be designated as auriculo-systolic (Cohn). Three types of these

A

B

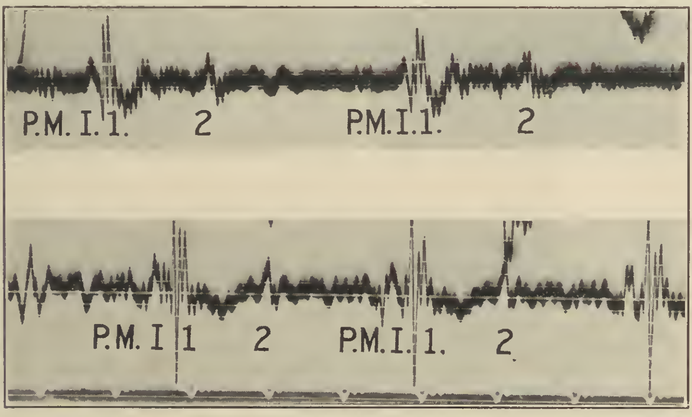

FIG. 116.—Phonocardiograms (direct method) from two cases of mitral stenosis. Upper record shows a presystolic murmur, *P.M.*, separated from the initial vibration, *I*, and the first sound, 1. Lower record shows a presystolic murmur, *P.M.*, merging with the initial vibration, *I*, and leading into the first sound, 1.

murmurs are recognized: (1) The presystolic murmur of mitral stenosis; (2) the Flint murmur; (3) a murmur of doubtful origin not associated with valvular lesions.

The presystolic murmur of mitral stenosis is the most obvious indication of this lesion as long as the auricles beat regularly and

appears with relatively mild grades of stenosis, in which no diastolic murmurs are present. The murmurs consist of a short increasing rumbling or purring, which appears to terminate in the clear and accentuated snap of the first sound. The vibrations are of large amplitude and so coarse that they can usually be appreciated as an apical thrill terminating in a forcible systolic impact. The murmur varies from time to time and for intervals may be absent entirely, being brought out by exercise, by lying on the left side (Pardee) or by inhalation of amyl nitrite (Morison).

Phonocardiograms of this murmur are interesting in several respects. In the first place, they show clearly that the presystolic murmur is not usually continuous with the main vibrations of the first sound, but precedes the introductory vibrations by a definite interval which the ear in auscultation fails to appreciate. This is especially well shown in Fig. 116, *A*. When the *As–Vs* interval is somewhat lengthened, it may have an apparently late diastolic position, as shown in Fig. 116, *B*. The initial vibrations occurring during the intersystolic interval are always unusually large and prominent. As a rule, the configuration of the first sound is also affected. Thus, in Fig. 116, *B*, the accentuated first sound is especially well shown.

FIG. 117.—Phonocardiogram (direct method) from case with a functional presystolic murmur, showing no presystolic vibrations but augmented initial vibration before first sound. Note also indication of third heart sound, 3.

The Flint murmur associated with the early diastolic murmur of aortic insufficiency was attributed by Flint to a vibration of the mitral valves, which are floated together by the regurgitation of blood. In other words, it may be regarded as a functional mitral stenosis. This explanation must be questioned in the light of more recent dynamic studies. It seems more probable that it is in some way associated with the greater ventricular distention at the time of auricular systole. Clinically, the murmur is distinguished by its decrescendo rather than its crescendo character, and does not run into a snappy first sound. Graphically, it is said to be distinguished by the fact that its vibrations are of greater frequency and that an interval never exists between it and the mid-diastolic murmur preceding it (Lewis). Finally, there may occur in structurally normal hearts, especially during excitement and in a standing position, a presystolic crescendo murmur simulating a brief presystolic murmur (Sewall, Morris and Friedländer, Lumsden, etc.). Often this is followed by a reduplicated first sound and so definite a systolic shock as to sug-

gest strongly mitral stenosis. As the murmur disappears upon lying down and is usually present in individuals with rather rapid hearts, it is not now regarded as of great significance by many clinicians, but it would be well, perhaps, to hold this conclusion in reserve. The writer had the opportunity at the U. S. Army Hospital in Lakewood to obtain phonocardiograms of a case so diagnosed by Dr. Morris. As shown in Fig. 117, no definite evidence of presystolic vibration at the time of auricular systole could be obtained after repeated trials. The graphic records do show, however, greatly accentuated introductory vibrations, which brings up the entire question as to how much of the auditory quality of presystolic murmurs is due to vibrations actually arising during auricular systole and how much to augmented introductory vibrations occurring during the intersystolic interval.

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CHAPTER XVII.

SPHYGMOMANOMETRY—THE CLINICAL ESTIMATION OF HUMAN BLOOD-PRESSURE.

APPARATUS, TECHNIC AND CRITIQUE.

All forms of blood-pressure apparatus in common use have three essential parts: The compressing cuff, the manometer and the inflating bulb or pump, together with a fine exhaust. If we desire to determine the diastolic pressure as well, some form of oscillometer is necessary.

The Compressing Cuff.—The arm-piece applied to the upper arm is composed of a rubber bag surrounded by an unyielding cuff. The bag should be made of fairly heavy rubber of good elastic quality. It should have a width of 12 cm. A narrow bag as originally used by Riva Rocci is generally supposed to yield too high readings. This is due (v. Recklinghausen) to the fact that pressure applied to a small area must overcome, not only the intra-arterial tension and the resistance of the arterial wall, but also the tension of the tissues; whereas, if the same pressure per unit area is applied over a wider space, only the outer pressures are concerned in overcoming tissue resistance, while the central pressure is transmitted directly to the arterial wall. This is illustrated by a diagram of v. Recklinghausen (Fig. 118). The bag may entirely encircle the arm, as is the case in most models of sphygmomanometers, or it may be a small bag 12 by 16 cm., as in the case of the Erlanger apparatus. It should be applied over the brachial artery on the inner aspects of the arm. Theoretically, the smaller bag, on account of its smaller volume of air, is preferable

The arm bag should be surrounded by an unyielding cuff preferably made of leather and fastened by suitable clasps. Some of the recent instruments have an outer covering of linen, which is not sufficiently unyielding to prevent an outward loss of pulsation. Owing to the smaller diameter of the limbs in infants and children, a smaller armlet is frequently employed. According to Judson and Nicholson, a cuff 9 cm. in diameter is necessary, however, between the ages of four to eight, while the adult size cuff should be used in older children. Occasionally, the thigh is used instead of the arm (Hill, Hoobler).

Critique.—It has not been universally accepted that a wide cuff is theoretically more desirable (Sahli). There can be no question that v. Recklinghausen's contention would apply if it were desired to obliterate an artery containing a constant pressure, or, in words of

the physicist, if "statics" alone were concerned. Such is not the case, however. The systolic pressure which we desire to measure exists only for an instant during each systole. Can an artery collapsed for a considerable distance *by a continued external pressure just equal to systolic be opened by the momentary equalization of intra-arterial and extra-arterial pressures?* It appeared from the results of arteriograph and physical experiments (Erlanger and Hooker) that this dynamic effect does not come into play enough to appreciably affect the readings even when the artery is compressed for a considerable distance. In more recent experiments, however, Erlanger found that the ability of the pulse to penetrate a stretch of artery is indeed a factor. He found that when the movements of several

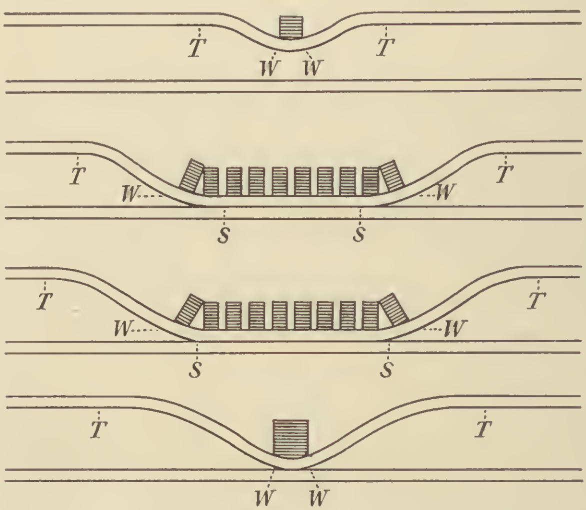


FIG. 118.—Scheme showing effect of equal pressures per unit area when applied over small and wide area of a collapsible tube. (After v. Recklinghausen.)

points of an artery stretched in a compression chamber were recorded, a systolic expansion of the more proximal portion of the artery occurred at compression pressures, which were 10 mm. higher than those which permitted the pulse waves to pass through the entire segment. As long as we have no information as to the length of the artery actually compressed by arm bags of conventional design, it is difficult to allow for the factors of resistance and pulse penetration in routine blood-pressure examination. Assuming, however, that only 4 cm. of the brachial artery is compressed, and, further, that the permeability of the brachial artery in man is the same as the femoral artery in the dog, it would follow, according to Erlanger's calculations, that the average systolic readings in man are about 8 mm. too low.

The Manometer.—The manometer may be a single limb, or U-shaped mercury manometer, a compressed air manometer or an aneroid pressure gauge. The one-limb mercury manometer consists of a reservoir of mercury into which a graduated tube dips or with the bottom of which it communicates. It was used on Riva Rocci's instrument and has been employed on many of its modifications (Cook, Stanton, Hill, Nicholson) (Fig. 119).

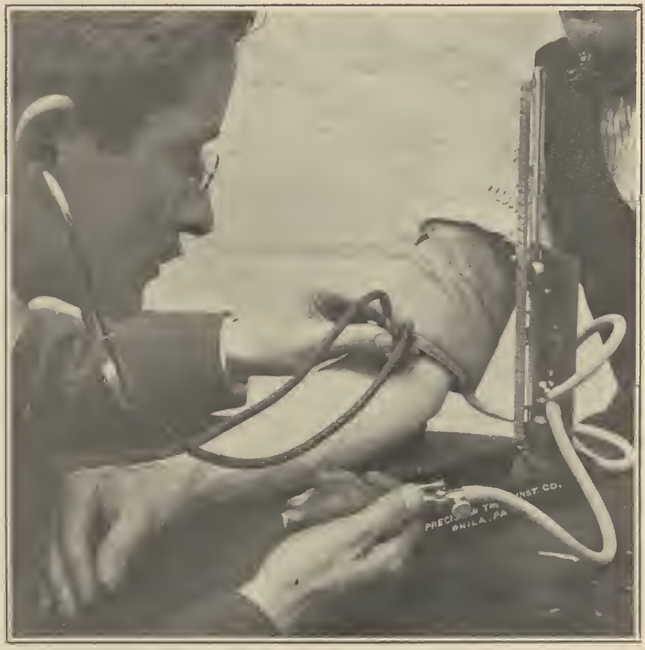


Fig. 119.—Nicholson's pattern of a one-limb mercury manometer. Method of auscultatory determination of blood-pressure. (After Norris.)

As the level of mercury changes or when it rises in the manometer tube, the scale must be corrected slightly, otherwise the reading is incorrect. In many of the earlier forms it was difficult to determine the exact zero level, owing to the depression of the mercury in the capillary tube, but this has been obviated in recent models.

The U-shaped mercury manometer has been utilized in many models (Janeway, Erlanger, Faught) (Fig. 121). The rise in one limb actually equals one-half the pressure change since the mercury in the opposite limb is depressed an equal amount. The scale is, therefore, less sensitive than the single limb manometers. It has the advantages of an easily determined zero level and of requiring only a small quantity of mercury.

The manometer tube should be made of heavy glass, of even caliber, and should have a length of about 40 cm. It should have sufficient damping so that the mercury does not oscillate, for otherwise the reading cannot be accurately made. This damping may be accomplished by reducing the caliber of the manometer tube to 2 mm., as in the Erlanger apparatus, or by introducing an artificial resistance, as in the modified Uskoff apparatus made by Zimmermann. This does not apply, of course, to those instruments in which the mercury

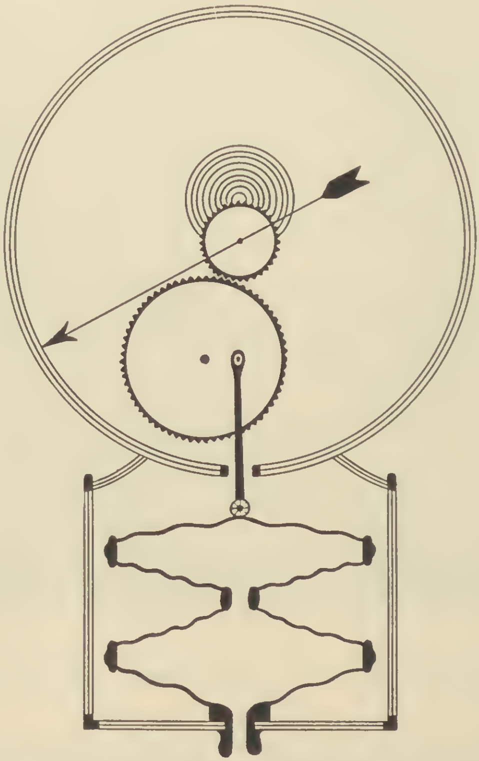


Fig. 120.—Diagram illustrating the construction of an aneroid instrument. (After Norris.)

is used to record the amplitude of oscillation as well (Janeway, Gibson). In this case a lumen of 3 or even 5 mm. is necessary.

Compressed air manometers consist of a sealed tube containing a globule of mercury or other liquid. As pressure is applied, the air enclosed is compressed and the globule serves as a guide on the calibrated scale. The principle has been used by Gaertner, Oliver, Hertz, etc. The effect of temperature changes must be obviated by compensatory adjustments or by enclosing the apparatus in a vacuum

tube of clear glass, as in Oliver's instrument. The chief advantage is their lightness and compactness; their chief criticism, that they are not sufficiently sensitive, *i. e.*, that only small movements of the index occur for considerable pressure variations.

Aneroid (*i. e.*, without fluid) manometers are of two types. They may consist of a chamber of corrugated metal which expands and acts upon a set of cog wheels actuating the hands which move over a calibrated dial (Fig. 120). To this class belong the Pachon, Tycos, Tagliabue, Sanborn and Pilling aneroids and the recording Jaquet sphygmotonograph.

A second type is made with a curved and hollow Bourdon spring, which tends to straighten when pressure is applied internally. The v. Recklinghausen tonometer is based upon this principle.

The pressure is increased in the system by introducing air with an ordinary atomizer bulb, a cautery bulb, a Pulitzer bulb or a metal pump. The large and clumsy pump used by v. Recklinghausen has never appealed to Americans. The pressure is reduced by letting out air by means of a fine leak. This may consist merely of a small opening over which the finger is placed, of a longitudinal slit, a screw adjustment or a special stop-cock. All tubing should be heavy walled and as inelastic as possible.

Oscillometers.—Devices for determining variations in amplitude with the sphygmomanometer are designated as oscillometers. The mercury or aneroid manometers recording the pressure may themselves fulfil this purpose, or a special device may be shunted into the circuit.

As already indicated, when the mercury manometer is employed to register oscillations, a wider tube than is otherwise necessary must be used. In many instruments the variations in amplitude are directly estimated (Janeway, Stanton). In others, a float, as in laboratory manometers, has been added (Gibson, Brugsch and Silbermann). Similarly, the needle oscillations of an aneroid may be read off and the regions of largest excursions estimated.

Various forms of oscillometers have been shunted into the sphygmomanometer system. Thus, v. Recklinghausen constructed a recording tonograph by utilizing a Bourdon spring which could be calibrated. Erlanger (Fig. 121) used a sphygmoscope system in which the pressure was prevented from acting on a delicate tambour by a rubber bulb, *B*, enclosed in a glass chamber, *G*. Similar devices are used by Muenzer, Wybauer and Uskoff.

The Fedde oscillator is a visual indicator of the amplitude. It consists of a tube containing a loosely fitting pith-ball which drops by its own weight during diastole, and during systole is sent up with an excursion proportionate to the amplitude of the pressure change in the system. The light weight of the ball and the absence of inertia add to the value of the instrument.

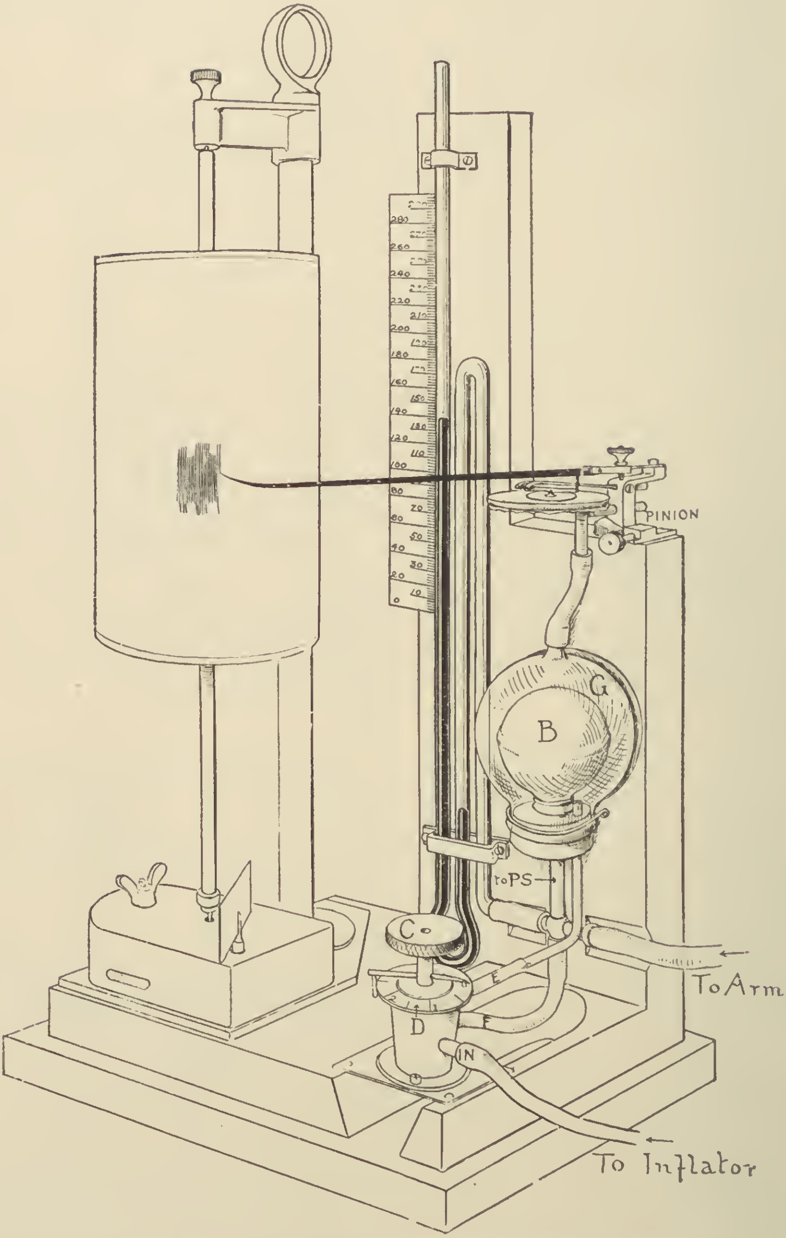


FIG. 121.—Diagram showing Erlanger's sphygmomanometer. (After Erlanger.)

Oscillations have also been visually estimated by the movements of a drop of fluid in a horizontal tube and in some forms the oscillations are transmitted from a separate cuff (Bing, Pal).

A separate aneroid oscillatory is included in Pachon's instrument. As shown in Fig. 122, the air-tight box, *B*, communicates with the air bag by tubes *f* and *d*. The pressure applied to the arm is measured by the manometer, *M*. The oscillations are transmitted to an expansile chamber, *a*, the pressure of which is maintained equal on two sides. The movements of this box are transmitted to the oscillometer needle, *n*.

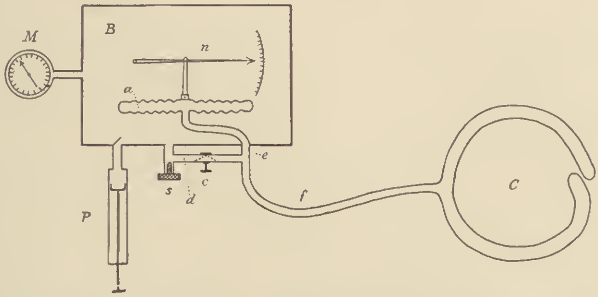


FIG. 122.—Diagram illustrating the construction of Pachon's aneroid oscillometer. (After Norris.)

Critique of Oscillometers.—The oscillations within the sphygmomanometer system occur because the sudden increase in volume of the arteries under the bag causes a temporary increase in pressure within the arm bag. We should not, therefore, be deluded into thinking, as is commonly done, that a constant extra-arterial pressure is playing on the arteries at any time. The pressure within the apparatus rises during systole and falls during diastole much as in the artery. The relation existing between the magnitude of these oscillations and those within the artery need not concern us here. It is pertinent to inquire, however, with what degree of accuracy the amplitude of the arterial wall oscillations are faithfully recorded by different oscillometers.

The mercury manometer is generally suspected of following the variations in amplitude very imperfectly. Its great inertia, indicated by its long vibration period, makes it a very inadequate mechanism. The practical dilemma usually arises, moreover, that the oscillations are either so small (which is the rule) that they do not serve a differential purpose, or so large (which is rare) that an accurate reading of the pressure is impossible. Were the manometer reliable, the lowest level would obviously represent the pressure exerted during diastole; but since the lower level is the resultant of two tendencies—the tendency of the instrumental inertia to place it higher and the combined tendencies of resonance and artificial

reduction of pressure to draw it down—it can be considered no more than a wild guess to locate the pressure exerted on the artery during the largest oscillations.

The statements made concerning the oscillatory mercury manometer apply, though with less force, to the aneroid patterns, the inertia of which is very much less. They are less apt, on account of their somewhat higher vibration rate, to undergo resonance effects. Of these the Pachon instrument, however, demands separate consideration, for in this apparatus oscillations are recorded by a separate aneroid (Fig. 122). This oscillatory aneroid is supposed to be constructed on ideal principles, for it purports to maintain the pressure on the internal and external surfaces of the drum, *a*, equal. In this way a very sensitive drum can be utilized and the sensibility is supposed to be constant at all pressures. Pachon seems not to have been aware of the fact that the sensitiveness is necessarily modified whenever air enters or leaves the system (see below), nor does he seem to recognize that the balancing of pressures during diastole is only approximate, a fact that could probably be remedied by introducing a minimal valve at *C*. The manometer, *M*, would then indicate the lowest pressure applied to the artery and the recording oscillometer would show the changes in amplitude. That it would do this very accurately, however, is questionable, since the lever has a vibration frequency of only 7 per second. The last statement also applies to the recording tonograph of v. Recklinghausen, which purports to record the form of the intra-arterial pressure curve. A mere inspection of the curve shows that this is not the case, however (Frank).

The oscillometer methods so far considered attempt to measure the qualitative pressure variations in the bag directly. In the case of the Erlanger, Uskoff and allied instruments, the oscillations are recorded through the intervention of a restraining ball or sphygmoscope system. In order that the oscillations of the lever shall correspond in amplitude to the pressure variations in the bag, it is necessary, first of all, that the ball expand by equal volumes for every equal increase of pressure. As Erlanger has shown, this occurs fairly evenly in the bulb utilized in his instrument, but it does not occur when a softer bulb restrained by a mesh-work is used, as in the Uskoff apparatus. The result is more unfortunate since the sensitiveness of the instrument increases precisely in the pressure field where the largest excursions are likely to occur.

Another factor, apparently not recognized by Erlanger, operates to change the sensitiveness at different pressures. As the pressure falls and air escapes, the elasticity coefficient of the air-containing bag decreases and the sensitiveness of the system gradually diminishes (Frank). Furthermore, the lever, the vibration frequency of which is only 6.5 per second, is inadequate to accurately pick up the

variations transmitted by the rubber ball. The advantages of the Erlanger apparatus are that oscillations of considerable amplitude are recorded and their sudden variations more clearly marked in the average run of cases than in other similar patterns. Furthermore, the damped mercury manometer allows an approximate estimate of the pressure applied to the artery during diastole. A more accurate measure of this could, perhaps, be obtained by the interposition of a minimal valve during the period in which the pressure is falling.

The Fedde pith-ball oscillometer is based upon an entirely different principle, namely, that a light particle in a tube within which pressure changes occur rapidly, will move in proportion to the force exerted by the pressure changes. On account of its lightness, it should prove a very accurate measure of the pressure changes within the bag. When the ball becomes rough or is no longer round, the tube causes it to adhere by friction. A careful and expert adaptation of the ball to the tube is imminently desirable. The chief drawback is that its movements cannot be recorded.

CRITERIA FOR ESTIMATING SYSTOLIC PRESSURE.

The Peripheral Pulsation Method.—*Riva-Rocci Method.*—The procedures now commonly employed consist: (1) In applying a circular arm-piece snugly to the bare arm, so that the bag lies on the inner aspect; (2) in inflating the system until the radial pulse disappears; (3) in gradually allowing air to escape through a fine leak and palpating for the first return of the pulse at the wrist. The reading of the mercury pressure at this moment is taken as systolic pressure. The procedure may be modified by recording the radial pulse by a sphygmograph instead of by palpation, but it is questionable whether the former is more sensitive. Or the brachial artery may be palpated instead of the radial, a procedure that has a theoretical advantage, since weak pulse beats are possibly smoothed out before they reach the radial artery. The advantage is probably offset by the fact that the brachial artery lends itself less easily to palpation. To make use of the advantage and negative the disadvantage, a smaller cuff has been snugly applied below the compressing cuff and, after inflating with moderate pressure, it is connected to some form of oscillometer (Bing, Pal, Hoobler). By this method it is possible to recognize pulsations peripheral to the bag at pressures from 3 to 10 mm. higher than by radial palpation. This procedure is especially valuable in children (Hoobler). The actual discrepancy between the two methods, of course, depends upon the acuteness of the tactile sense, as well as upon the sensitiveness of the oscillometer.

Principle.—The principle of using the first evidence of a returning pulsation peripheral to the compressing bag as a criterion of systolic pressure is based upon the supposition that as long as a pressure

greater than systolic is exerted on the artery, it remains collapsed during systole as well as during diastole; but as soon as extra-arterial pressure equals or falls slightly below intra-arterial systolic, it allows blood to pass during systole and gives rise to a peripheral pulse. This dictum presupposes: (1) That the arterial wall offers no appreciable or, at least, a constant resistance to compression; (2) that the artery compressed for a considerable length can be opened by the systolic pressure, which acts only momentarily; (3) that the first blood passing into the peripheral vessels can cause a pulse wave. All of these suppositions have been questioned. The second has already been discussed.

As a compression pressure is applied, arteries like elastic tubes tend to collapse in the middle, but leave small gaps on the sides. To completely close these, requires a pressure in excess of that found within (Christen, Brooks and Luckhardt).

The related question has frequently been discussed whether sclerosed vessels offer more resistance to compression (Russell) than normal arteries. Experiments indicate that while a thickening or calcification does not appreciably increase the resistance of vessels to compression (Janeway and Park, MacWilliam and Kesson) a high state of tonic contraction may offer considerable resistance, and by reducing the lumen of the vessels may also interfere with the peripheral transmission of the systolic pressure wave (MacWilliam).

In regard to the third supposition, it can readily be demonstrated that when the forearm is enclosed in a plethysmograph, its volume begins to increase before pulsations are visible either in the plethysmograph recorder or in a second arm bag. It would appear, therefore, that the application of an equisystolic pressure to the arm causes merely a stenosis, through which blood may seep at the height of systole, but in amounts not sufficient to cause a pulsation. It appears likely, therefore, that a return of a peripheral pulsation large enough for recognition occurs only when the extra-arterial pressure is less than intra-arterial systolic. Experimental evidence in favor of this has, furthermore, been adduced by Erlanger (*cf.* page 336).

Comparison with the plethysmograph method indicates that this error may be equal to 10 or 15 mm. of mercury in man, and comparisons with the direct pressures obtained in animals also indicate that the systolic pressure is greater than that estimated (Fellner and Rudinger, Erlanger, Wiggers, Eberly and Wenner). Comparisons of these pressures with the intra-arterial pressures in man directly estimated by the Hürthle manometer indicate an opposite relation, namely, that the intra-arterial systolic is less than that estimated by palpation (Müller and Blauel). Too great stress should not, however, be placed upon these results, which were apparently obtained on three individuals by types of direct manometers, themselves not free from errors.

The Auscultatory Method.—The method of auscultation suggested by Korotkow (Fig. 119) utilizes the appearance of a sharp sound peripheral to the bag as a criterion of systolic pressure. The procedure adopted is as follows: After compressing the brachial artery by means of a pneumatic bag in the usual manner, a stethoscope bell is applied over the brachial artery below the armlet or in the cubital fossa. As the pressure is gradually released and the artery decompressed, a faint sound is heard at the moment that the artery becomes permeable to the pulse beat. Actual comparisons have shown that the first sound is heard at pressures from 5 to 15 mm. higher than those which permit a pulse to pass to the wrist (Korotkow), yet it occurs almost synchronously with the graphic criterion for systolic pressure (Fig. 123). The mechanisms concerned in the production of this sound are discussed later (*cf.* page 351).

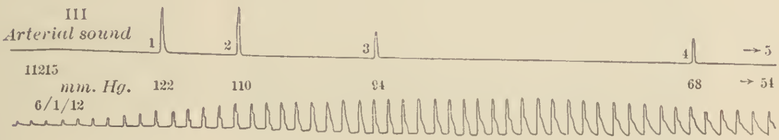
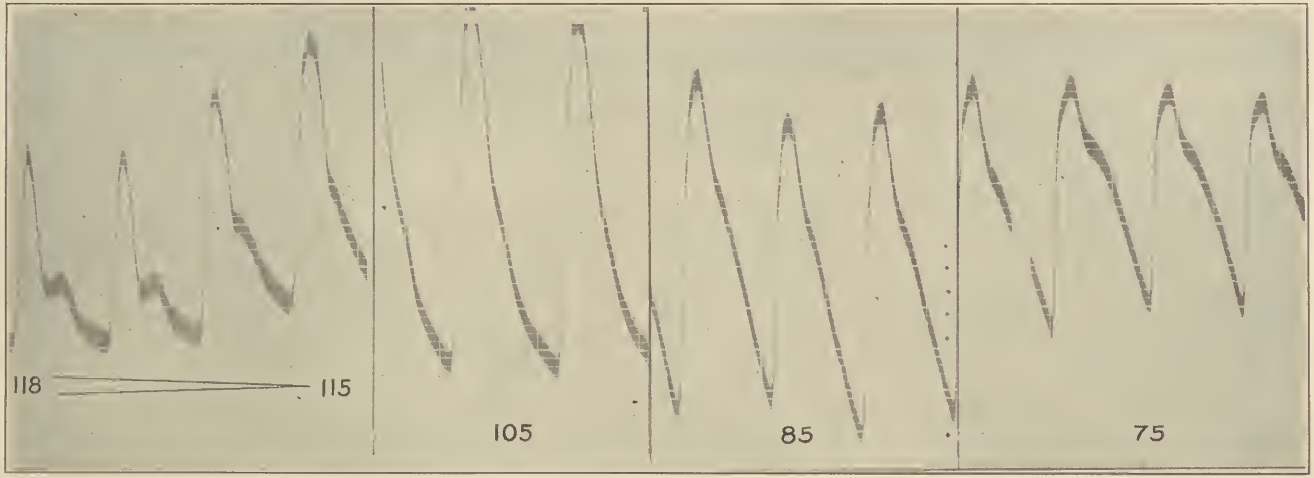


Fig. 123.—Curves showing the relation of amplitude of oscillation to different phases determined by the auscultatory method. (After Norris.)

The Oscillatory Method.—The pressure at which oscillations in the manometer system first occur has been suggested as a criterion of systolic pressure on the supposition that they appear only after blood has been forced under the bag (Pachon, Uskoff). It has been established, however, that such oscillations occur at pressures far in excess of systolic, due to the "ram action" of the occluded artery upon the bag (v. Recklinghausen, Erlanger). Evidently their incidence is no criterion for systolic pressure, the relative time of occurrence depending entirely upon the sensitiveness of the apparatus.

When blood actually passes under the bag and the heaving sensation is noted, *the recorded waves become larger and change their character at the same time that the base line rises.* The abrupt and simultaneous occurrence of these changes has, therefore, been suggested by Erlanger as a criterion of systolic pressure (Fig. 124). Practically, neither the rise of the base line, which depends upon the size of the leak in the tambour, nor the sudden increase in amplitude has met the expectation as a criterion. Frequently, the increase in size is either not sudden, but gradual and progressive, or several abrupt changes in amplitude occur. The change in the shape of the curve is, however, a valuable criterion. The change in the conformation of the wave (Fig. 124) consists in the fact that a wave (dicrotic?) becomes supported on the descending limb, which gives an effect,



A *B* *C* *D*

Fig. 124.—Four segments of tracings from Erlanger's sphygmomanometer obtained by substituting an optical capsule as recording mechanism. *A*, four criteria of systolic pressure—larger oscillations, rise of base line; support of notch on descending limb, separation of base line; support of notch on descending limb, separation of base line; reflected wave of v. Recklinghausen. *B*, maximal oscillations. *C*, first decrease. *D*, final decrease. (Opinions are still at variance as to whether *C* or *D* indicates diastolic pressure.) Figures refer to pressures at which curves were recorded.

when written on the slowly moving drum as if the bases had been separated.

What is the explanation of these changes? The rise in the base line has been accounted for by the fact that, when more blood rushes under the bag, the base line is elevated before the pressure in the tambour can be equalized through the small leak. The amplitude is increased because a stretch of artery pulsates under the arm bag. This increase is often not abrupt, but presents an increasing series of waves due to the fact that the pulse penetrates the length of the compressed segment gradually (Erlanger).

The change in shape demands a fuller explanation. As long as the oscillations are due to a "ram action," the recorded pressure is the expression of a sudden shock, rising and falling rapidly together with a small reflected wave. As soon as blood passes under the bag, the fall occurs more slowly because blood must be squeezed out during its fall (Erlanger). Experience indicates that the systolic pressure determined by this criterion averages from 5 to 15 mm. higher than that determined by palpation, while it is synchronous with the first sound heard on auscultation (Fig. 123).

CRITERIA FOR ESTIMATING DIASTOLIC PRESSURE.

Amplitude of Oscillations Peripheral to the Bag.—If the pressure is gradually released from the arm bag and the radial pulse palpated (Strasburger), or, better, if the radial pulse is recorded by a sphygmograph (Janeway, Massing, Sahli, Jaquet), it will be found that the amplitude increases until a certain maximum is reached, after which no further increase in size occurs. A similar increase in oscillations up to maximal may be observed in the excursions of an oscillometer, which is connected to a second arm bag applied below the compressing bag (Janeway, Clark, Bing, Vaquez, Oliver, etc.). The point at which the oscillations peripheral to the bag become maximal has been used as a criterion of diastolic pressure.

This criterion is based upon the principle that the quantity of blood which is allowed to pass through the arm bag and, hence, the pulse amplitude, depends upon the compression of the artery. Thus, if the extra-arterial pressure were 100 mm. (Fig. 125), the artery presumably would not open until the intra-arterial pressure during systole had passed 100 mm. It remains open and allows a pulse wave to pass peripheral to the bag so long as the pressure remains above this level during systole and subsequent diastole. For this reason a small pulse wave is recorded, as indicated by the heavy lines.

As the extra-arterial pressure gradually falls and the intra-arterial diastolic pressure is approached (say 80 mm.), the artery beneath the bag remains open during the entire interval of diastole and allows a maximum pulse wave to be propagated. Since a further reduction

in the external pressure could not lengthen the interval that the artery remains open, no further increase in the amplitude occurs.

The criterion is open to an essential criticism, however, viz., that the amplitude of the peripheral pulse is determined, not only by the amount of blood passing under the bag, but also by the volume-elasticity coefficient of the artery, which depends largely upon the volume of blood in the peripheral arteries. When both venous efflux and arterial influx have been shut off, the blood tends to pass from the higher arterial to the lower venous pressure, and, hence, tends to leave the arteries so that the pressure within them becomes

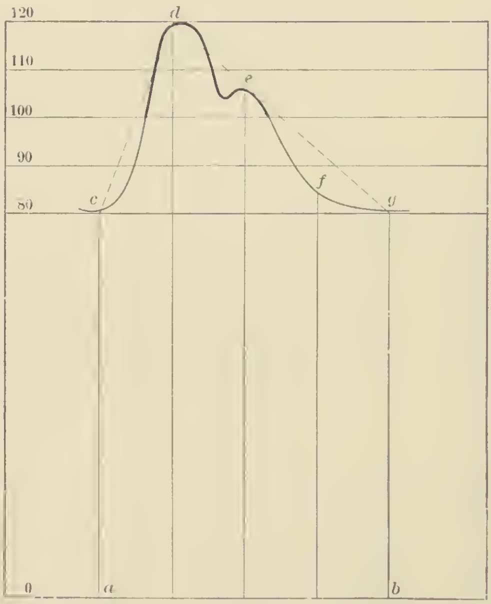


Fig. 125.—Diagram illustrating the utilization of the amplitude of the peripheral pulse as a criterion of diastolic pressure. (Norris.)

low. As soon as blood reënters the forearm and causes pulsations of a small amplitude, it raises the peripheral pressure during every beat and decreases the volume-elasticity coefficient. The effect is that, for equal volumes of blood entering, there is always less and less excursion of the artery. There are, then, two forces at work, the greater systolic filling of the artery tending to reduce the amplitude, and the greater volume entering per beat tending to increase it. For a long time the latter overpowers the former. It is quite possible, however, that when the arm bag contains an extra-arterial pressure somewhat above actual diastolic, these two forces counterbalance. Then, no further increase in amplitude occurs. This may explain

why the readings of the diastolic pressure thus obtained are always considerably above those obtained by other methods. The varying pressure of the sphygmograph button which exists when the artery fills also seriously affects the accuracy. It is well known that the amplitude of excursion recorded by the sphygmograph depends upon the relation of intra-arterial pressure to extra-arterial tension. As the former gradually rises, and the arterial volume increases, this relation may be improved or made worse, depending upon the adjustment of the apparatus. It is, therefore, not surprising that widely differing results have been obtained and the method has not been generally accepted as reliable.

Amplitude of Oscillations within the Arm Bag.—If, while the pressure is slowly falling within the manometer system, the oscillations from the arm bag are graphically recorded, as in the Gibson, Erlanger, Uskoff and similar apparatuses, or are observed in the swing of a mercury column, an aneroid pointer, or any other oscillometer, the oscillations will be seen to increase in amplitude, remain at a maximum for a considerable time and then gradually (more rarely, abruptly) decrease. *The extra-arterial pressure at which the oscillations are largest was first suggested as a criterion of the diastolic pressure* (Erlanger and Hooker). It is quite generally stated that the principle on which this criterion depends is that of Marey. It was Marey who first laid down the principle that an artery oscillates with greater amplitude as the pressure increases up to a certain level. He assumed that when the internal and external pressures are equalized, the arterial wall is relieved of tension and is in condition to oscillate freely. Such an equalization of tension causes a greater excursion, according to Frank, because the volume-elasticity coefficient $\left(\frac{\triangle p}{\triangle v}\right)$ of the wall is reduced, and, *hence, the sensitiveness of the entire recording system, of which the arterial wall is essentially a part, is thereby increased.*

The mechanical experiments upon excised arteries, rubber tubes and arteries in connection with the circulation (Mosso, Howell and Brush, Erlanger) have been considered as demonstrating conclusively that the largest oscillations may be used as a criterion of diastolic pressure. All of these investigators, no matter how careful their technic, have been obliged to register the actual pressure variations by the apparatus available at their respective periods. Thus, Mosso was forced to content himself with the mercury manometer, Howell and Brush with the Fick spring manometer, while Erlanger used maximum and minimum valved manometers. All of these are now known not to be devoid of error. It cannot, therefore, be accepted as demonstrated beyond doubt that the largest oscillations do occur when an exact equilibrium is reached between intra- and extra-arterial pressure. Recent work has, moreover, tended to cast doubt upon

the dictum that the largest oscillations occur when extra-arterial pressures are equal to diastolic within the vessel. Thus, MacWilliam and Melvin, on the basis of physical experiments upon excised arteries, find that, with normal elastic arteries, the maximal oscillations occur when the external pressure is sufficient to produce what they term a "half-flattening" of the artery, *i. e.*, a state in which the short diameter is roughly one-half that of the distended tube. The natural inferences from such experiments are that the pressures at which largest oscillations occur must be considerably above diastolic, while the point at which subsequent reduction in amplitude occurs more accurately corresponds to diastolic pressure. In agreement with this view is the theoretical exposition of Christen. He points out that whenever a tube of an elastic nature is expanded by equal pressure increments, it will be found that at first the expansion is small, then becomes suddenly greater and, after the distensibility has remained constant, grows smaller again. The tube may be said to pass through three elastic fields: the first, in which the distensibility is small, the second, in which it is great, and the third, in which it decreases again.

Arteries in their normal condition are always in the third field of elasticity, which accounts for the fact that the excursion of the wall is so slight. When an extra-arterial pressure is applied, however, which somewhat exceeds the intra-arterial diastolic pressure, the artery shifts to the second field of elasticity, *i. e.*, the one in which the volume-elasticity coefficient is small and the oscillations large. When the extra-arterial pressure is lowered to the point where it exactly falls below the intra-arterial pressure, the arterial wall enters the third field of elasticity again and the oscillations become smaller. The suddenness of the change is determined by the nature of the artery—the more resistant the vessel, the more gradual the change in amplitude.

On the basis of physical experiments, Brooks and Luckhardt were unable to establish the validity of the Marey principle, even as applied to simple membranes and tubes, and concluded that the maximal oscillations occur when the mean pressures within the artery equal the mean pressures around it. In similar experiments, Erlanger (1916) was also forced to conclude that maximal oscillations can occur at diastolic or even systolic compression pressure, but believed that this is due, among other things, to the fact that the configuration of the pressure pulse is determined by: (*a*) The compressibility of the compression space, and (*b*) by the phase of the pulse cycle that the compression chamber is closed. Such results make it obvious that the deductions from purely physical experiments may not be transferred without great care to conditions occurring within the arterial system, where pressure variations of a distinctive nature occur.

In more recent experiments (1921), in which variations in the radial amplitude of the artery were directly recorded at various extra-arterial pressures, Erlanger found that the diastolic form of the artery at the time of the largest excursion, while never completely flat, depends upon the number of factors, *e. g.*, the duration of the pulse cycle, resistance to outflow, etc., which vary from one estimation to the other. He consequently quite properly concluded that, judging by the behavior of the radial amplitude of oscillations, the diastolic pressure is balanced by the extra-arterial after the point of maximal oscillation (Erlanger's early criterion) but before their abrupt diminution (MacWilliam's and Melvin's criterion) or more specifically at the point "where the accelerating decrease in amplitude of the sphygmomanometer oscillations changes to a retarding decrease."

This also accords with the results of animal experiments, in which the pressure is applied to the leg of a dog by a conical cuff prevented from slipping by special devices (Lang and Manswetowa, Wiggers (unpublished). In such instances the maximal oscillations always occur at extra-arterial pressures considerably above measured diastolic.

The Auscultatory Method.—If the chest-piece or bell of a stethoscope is applied over the brachial artery, below the cuff of any blood-pressure apparatus (Fig. 119), a series of sounds can be heard as the pressure gradually escapes. The changes in the sounds may be divided into five phases, the relations of which to the oscillatory changes are shown in Fig. 123.

First phase: The sudden appearance of a clear sound, lasting for a fall of approximately 14 mm. of mercury. This has already been described as a criterion of systolic pressure.

Second phase: The acquisition of a murmurish character, lasting while the pressure falls approximately 20 mm. of mercury more. It is attributed to the stenosis of the vessel produced under the cuff at this stage.

Third phase: The replacement of the murmur by a sound becoming progressively louder and lasting during the next 25 mm. of pressure fall.

Fourth phase: The muffling of the sounds, lasting while the pressure falls 5 to 6 mm. more. The cause of this muffling has been variously interpreted as due: (*a*) To the absence of diastolic collapse; (*b*) to the slowing of the stream under the cuff; (*c*) to the decreased resonance in the deflated cuff; (*d*) to a lack of flattening of the arterial wall (MacWilliam and Melvin).

Fifth phase: The disappearance of all sound.

Mechanism of Production of Korotkow Sounds.—A number of different explanations have been given as to the cause of the Korotkow sounds. They may be briefly summarized as follows:

1. That the sound is produced in the empty artery beyond the compression (Korotkow, Gittings, Howell and Goodman, Ehret).

According to this view, the sounds are due to "the forcing apart of the arterial wall by the first stream of blood which reaches the artery below the cuff." The lower part of the brachial artery during compression is practically empty and the sudden stretching of the artery by the first stream of entering blood is supposed to be responsible for the sound. Korotkow offers in support of this explanation the fact that a sound is produced when liquid is poured into an empty iliac artery. Since the Korotkow sounds can still be obtained, however, when the artery is occluded just peripheral to the point of compression, as well as when the artery below is distended with blood, this explanation becomes improbable (MacWilliam and Melvin, Erlanger).

2. That the sound is produced by changes in the form of the tube under compression (MacWilliam and Melvin). According to this view, the sudden change in form of the artery under compression is the cause of the sound waves. In its support, MacWilliam and Melvin bring forward the evidence that a strip of excised artery in a compressed chamber gives rise to characteristic sound vibrations when it is compressed.

3. That the sound is due to the vibrations of the entire mass of tissue under the compressed area. In the words of Flack, Hill and McQueen, the compressed area of the arm is converted "into a resonating mass, the pulse is not damped down in the labile arteries, but strikes the blood which fills to distention not only the main artery but every patent arteriole throughout the mass and causes the whole tense mass to vibrate." This explanation is invalidated by the fact, however, that the bare artery suffices for the production of sounds (MacWilliam, Erlanger).

4. That it is aided materially at least by the resonance effect of the arm bag (Gittings). In support of this contention is cited the observation that a similar compression of arteries by an Esmarch bandage produces only comparatively feeble sounds. This may, however, be due to a greater limitation of the movements of the arterial walls under compression (Erlanger).

5. That the sounds are due to a water-hammer action (Erlanger). The explanations previously cited are neither free from objections nor do they explain in detail why the character of the sounds changes and why they finally disappear during decompression. By "water-hammer" is meant the powerful pressure-effect produced when the motion of a mass of fluid is suddenly checked, and the water-hammer theory would compare the sound production in a compressed artery to the same effect as that which causes the well-known sound in a water pipe when a flowing faucet is suddenly closed. In detail, the following events are pictured by Erlanger as occurring when the artery is gradually decompressed: "(*a*) The first sound is heard at the instant the blood in the artery below the compression chamber shows a

brusque acceleration with each pulse. (*b*) The intensity of the sound then increases through the second and third phases as long as the diminishing compressing pressure still suffices to occlude the artery during a part of diastole. It is during this stage that the energy liberated by the water-hammer presumably is constantly increasing. (*c*) The sudden dulling and weakening of sound (fourth phase) occurs exactly at the instant the compressing pressure leaves the artery open during diastole. On the basis of the water-hammer hypothesis, this weakening is due, not alone to a diminution in the velocity of flow into the compression chamber during systole, but perhaps even more to the fact that the column of blood below is no longer stationary at the time it receives the impact but is moving continually in the direction the impact tends to drive it. (*d*) Below the diastolic level of compression the sounds usually soon fade way (fifth phase). Even at this time, however, some water-hammer action must still persist, for the artery in the compression chamber still increases in volume with each pulse more than does the uncompressed artery. The more rapid flow thus permitted in this part must be checked by the more slowly moving blood below. It is scarcely necessary to add that in those instances in which the pulse itself is brusque enough to elicit sound vibrations from the artery, the sounds will persist even when the artery is relieved of all compression."

This theory would explain also the well-known persistence of the sound in aortic insufficiency when very low or even no extra-arterial pressure is applied. The evidence in favor of this hypothesis is summed up as follows by Erlanger:

"(*a*) While sounds are in evidence, blood enters the compressed artery with a velocity far in excess of the normal.

"(*b*) When the sounds are loud (third phase), the artery in the compression chamber can be made to act as a hydraulic ram through the peripheral artery.

"(*c*) The pressures central of the compressed artery (circulation schema) fall while the wider compression oscillations are recording.

"(*d*) The configuration of the compression pulse conforms with the requirements of the water-hammer hypothesis.

"(*e*) The sounds are located in that phase of the pulse cycle in which a water-hammer would strike.

"(*f*) The intensity of the sounds varies during decompression as the values obtained from records assumed to indicate the force of the water-hammer.

"(*g*) Calculation locates the initial site of sound production in the lower end of the compression chamber.

"(*h*) That the sound is produced by a sudden impact is indicated by the fact that the first of the series of vibrations associated with each sound is the highest.

"(*i*) The form of the pulse beyond the compression chamber is such,

in certain stages at least, as could be produced only by a sudden impact more forcible than any the pulse itself could strike.

"(*j*) The sounds are loudest at the lower edge of the compression chamber.

"(*k*) The sensation perceived in the arm during the systolic-diastolic phase of decompression is localized where water-hammer would strike and has the characteristics of a blow delivered by water-hammer."

Practical Criterion of Diastolic Pressures.—Although Korotkow and his followers at first utilized the disappearance of all sound as a criterion of diastolic pressure, some doubt has arisen as to whether the entire disappearance of sound or the fourth phase first described by Ettinger, in 1907, represents the correct criterion. Numerous investigations have been instituted to determine this question. With a few exceptions, these have consisted in comparing the pressures read at the fourth and fifth phases with other criteria. The work may be summarized in the following table:

Investigator.	Year.	Phase found to be criterion.	Method of experimental determination.
Korotkow	1905	5th	Experimental determination.
Ettinger	1907	5th	Janeway-Masing comparison.
Lang and Manswetowa .	1908	4th	Oscillatory method of von Recklinghausen.
Lang and Manswetowa .	1908	4th	Comparison with Hürthle diastolic in the dog.
Van Westernrijk . .	1908	4th	Oscillations of Pal's sphygmoscope.
Fisher	1908	4th	von Recklinghausen's oscillatory method.
Ehret	1909	5th	Oscillatory method.
Gittings	1910	5th	Visual and oscillatory.
Goodman and A. Howell	1910	5th	Oscillations of mercury manometer.
Hoover	1910	4th	
Warfield	1912	4th	Animal experiments.
	1913	4th	Erlanger oscillatory method.
Weysse and Lutz . .	1913	4th	Decrease of oscillations of Erlanger apparatus.
Dehio	1912	4th	Sphygmograph method.
Oliver	1911	4th	Oscillations of spirit indicator.
Taussig and Cook . .	1913	4th	Oscillations (Erlanger).
Hooker and Southworth	1913	5th	Oscillations (Erlanger).
MacWilliam and Melvin	1914	4th	Experiments on excised arteries.
Erlanger	1921	4th	Experiments on exposed arteries.

The perusal of the foregoing table indicates that the consensus of opinion favors taking the fourth phase as a criterion of diastolic pressure. This has a distinct advantage in clinical work, since in many cases a total disappearance of sound does not occur (*e. g.*, aortic insufficiency).

On the other hand, different observers will be found to agree more closely upon the pressure level at which all sounds cease than they will upon the pressure level at which a muffling occurs.

The method has been further studied in relation to the changes that occur during abnormal conditions of the circulation (Goodman and

A. Howell). Until we have more fundamental knowledge as to the factors concerned in the alteration of such sounds, it is, however, unwise to attribute much significance to them. During arrhythmias the variation in the strength of succeeding systoles may be studied and compared with pulse-tracing amplitudes. The fifth phase is filled by a continued sound in cases of aortic insufficiency (Taussig and Cook).

Movements of the Artery during Decompression.—In order to gauge the relative reliability of the various criteria suggested for the determination of systolic and diastolic blood-pressure, it is important to gain as clear an insight as possible into the variations in size which an artery undergoes during consecutive moments of each systole and diastole and during progressive decompression.

Hypothetical considerations indicate that when the extra-arterial pressure is higher than diastolic, but lower than systolic, the following changes occur during each cardiac cycle: As soon as the intra-arterial pressure during systole exceeds extra-arterial, the arterial wall tends to move abruptly from a position of complete collapse to a "just round" or "zero" size. The higher the extra-arterial pressure, the later this occurs after systole has begun. The rapidity of change is somewhat retarded, however, by inertia and by friction which is offered to the penetration of the blood into the collapsed artery. During the remainder of systole, the artery is further distended in proportion as the systolic intra-arterial pressure from moment to moment exceeds the compressing pressure in relation to the distensibility of the arterial wall. Similarly, it may be supposed that the arteries collapse suddenly as soon as extracardial pressures exceed intra-arterial. Owing to the resistance against which the segment must empty itself, together with the inertia of the blood to be overcome, such collapse probably does not occur suddenly but rather gradually.

Valuable as such theoretical considerations are, valuable as are also experiments on artificial models, it is obvious that the real changes in arterial size must, in the end, be determined by carefully controlled direct experimental work on animals. Such an investigation was undertaken by Erlanger, who devised methods for photographically recording the movements of the exposed artery of a dog while and where it was in the process of decompression, as in making blood-pressure observations on man. Records so obtained have established the following interesting facts (Erlanger):

Before the pulse succeeds in penetrating the full length of the segment under compression, a thin layer of blood is pushed through the completely flattened segment, but with progressive decompression it penetrates about 1 cm. farther with each 2.7 mm. Hg. decrement until it penetrates the entire segment. Attention has already been called to the obvious error this behavior of the pulse, relative to the

width of the armlet, introduces into all systolic readings of the blood-pressure. The gradual penetration of the pulse during decompression explains the absence of a *sudden* increase in amplitude of oscillations in oscillometers and suggests that the first penetration of the pulse in the compressed artery is indicated in oscillometers by a rapid but not necessarily a sudden increase in the amplitude of oscillations.

When the pulses begin to travel through the segment a diastolic residuum for a time accumulates rather rapidly, owing to the fact that the time elapsing between pulses is insufficient for the compressing pressure to completely empty the segment of blood. Shortly before the time when the third phase of the sounds changes into the fourth phase the diastolic remainder again accumulates rapidly, but, beginning with the sounds of the fourth phase, the diastolic residuum increases less rapidly, indicating that the filling of the artery has reached a point where the walls remain stretched during diastole. Variations in the excursions of the compressed segment indicate that the oscillatory index of diastolic pressure is not the first sudden diminution, but the point where the accelerating diminution in oscillation amplitude begins to give way to a retarding diminution.

In the stage of decompression, during which the artery is partly flat (*i. e.*, from the time when the pulse first begins to penetrate the length of the segment up to the time of the fourth sound phase begins), there is in evidence a process which Erlanger has designated the *pre-anacrotic phenomenon:* The pulse front increases in steepness as it progresses through the flattened artery and small pre-anacrotic waves develop in front of it, the one immediately preceding the anacrotic limb usually being negative and undergoing an interesting metamorphosis.

Continuous or Serial Blood-pressure Determinations in Man.—In order to obtain an idea of blood-pressure fluctuation from time to time, a number of appliances have been introduced, each of which uses one or the other of the foregoing criteria of blood-pressure determinations.

Erlanger probably devised the first practical procedure by means of which blood-pressure fluctuations may be made evident from time to time. After the cuff has been applied to the arm the extra-arterial pressure in an Erlanger sphygmomanometer system is set at a pressure slightly above diastolic or slightly below systolic and a continuous record is taken. As the amplitude as well as the contour of waves is determined by the relation between intra-arterial and extra-arterial pressures, any change in amplitude may be interpreted as an increase in systolic or diastolic pressure as the case may be. A similar method was used by Groedel, who employed the Uskoff sphygmomanometer. The length of time that the compression cuff may be kept inflated without unbearable discomfort is, of course, limited and no absolute readings are possible. Furthermore, there is some question as to whether the amplitude of oscillations is fundamentally indicative

of changing diastolic and systolic pressures or whether they may not alter predominantly with changes in pulse pressure (Wiggers).

Fantus described a modification of the Erlanger apparatus, by which repeated observations of the *actual* systolic and diastolic pressures may be correctly made at as short intervals as are required for the rapid inflation and the slow deflation of the Erlanger system. The Erlanger criterion of systolic and diastolic pressures is used.

Blankenhorn devised an apparatus which is designed to record series of systolic and diastolic pressures automatically and at stated intervals. At stated and set intervals, a sphygmomanometer system connected to the patient by a cuff is automatically inflated from a pressure tank. Two mercury manometers are used—one recording the pressure, the other the amplitude of oscillation. The latter writes horizontal strokes on the drum as the pressure gradually falls. From these oscillations, systolic and diastolic pressures are read according to oscillatory criteria. While no doubt serving the clinical purposes for which it was designed, its accuracy is limited by the fact that it utilizes a mercury manometer as an oscillometer (*cf.* page 341).

Finally, Kolls presented an ingenious assemblage of apparatus by means of which continuous pressure records can be obtained in man. The apparatus consists of a double cuff attached to an apparatus similar to that of an Erlanger sphygmomanometer, with the exception that the mercury manometer is of larger bore and equipped with a float and pointer writing on a drum. Through an electro-magnetic valve, the pressure within the two cuffs is so controlled that the pressure in the lower cuff connecting with the recording manometer is always approximately equal to that required to obliterate the artery and, consequently, writes continuous records when that pressure is approximately systolic. With every pulsation that strikes the lower cuff, a small amount of air is directed into the upper one, thus tending to elevate the extra-arterial pressure. When, however, pulsations do not escape beneath the upper cuff, a small amount of air escapes from it and the pressure within this system falls.

PRACTICAL ASPECTS OF BLOOD-PRESSURE DETERMINATIONS.

Choice of Apparatus.—Before selecting any form of apparatus, the principles it is desired to utilize should be chosen. This applies largely to the estimation of diastolic pressure. For general practice, the auscultatory method is in all respects the best. It may be carried out with any form of apparatus. The oscillatory method of recording diastolic pressure is peculiarly adapted to hospitals and office work. Among the forms of apparatus utilizing this criterion, those employing a direct recording spring manometer (as those of v. Recklinghausen and Jaquet) are probably preferable to those using a sphygmoscope

system, as the Erlanger, but the latter, in turn, is more accurate in construction than the Uskoff. Visual oscillatory methods are less satisfactory, because the point at which large oscillations cease can be only approximately gauged. Those forms of apparatus in which the largest oscillations occur are best. The Fedde and Pachon oscillators are, therefore, preferable to those of Hill, Bing, etc. Instruments that read the oscillation with the manometer recording the pressure, as the Gibson, Janeway and other mercury models, as well as the spring aneroids, are not to be recommended for determining diastolic pressure by the oscillatory method.

Having selected an instrument adapted to operate upon the principle chosen, attention should next be directed to its accuracy and workmanship. The scale should be correct and adjustable; the zero level readily verifiable. The system should be free from leaks; the tubing of heavy quality; the bag elastic, 12 cm. wide and not too long, but above all protected by a rigid unyielding cuff.

Portability is a great consideration, but accuracy should never be sacrificed on its account. Aneroid manometers, while convenient, are liable to become inaccurate and to need recalibration.

The Patient as a Factor in Accurate Determination.—The pressure should always be taken in the same position, recumbent or sitting, and, if in the latter, the arm bag should be placed on a level with the costosternal angle. The arm bag should be applied loosely so that a small volume of air remains within when the manometer is at zero, but tightly enough so that this contained volume of air is not too great. It is desirable to make the determination as rapidly as possible in order to avoid or minimize a direct mechanical or reflex effect on the general blood-pressure. If meals, warm drinks, alcohol, tea or coffee have been partaken of shortly before the blood-pressure measurement, or if exercise or smoking has been indulged in, their tendency to elevate pressure should be taken into account, as should the psychic reaction of the patient. The following sequence of procedures suggested by Norris probably adequately guards against psychological errors on the parts of both examiner and patient: "(1) Discard the results of the first reading, using it simply to demonstrate the harmless and painless character of the procedure, and, when possible, make subsequent readings after some little time has elapsed. (2) Avoid making blood-pressure observations when the patient is excited, anxious or worried, as a result of an examination, etc. (3) Make several consecutive readings and, *if they correspond more or less closely*, take the arithmetic mean. (4) Make the observations as quickly as is consistent with accuracy; do not look at the manometer until the pulse is felt (or a certain phase of sound heard on auscultation)—at this point the air escapement should be tightly closed until the reading is made. (5) Allow the pressure to fall to zero between observations and permit sufficient time to elapse between readings for the venous pressure (stasis) to fall to the normal level."

CLINICAL VALUE OF BLOOD-PRESSURE DETERMINATION.

Normal Variations.—Before it is possible to attribute pathologic significance to blood-pressure readings, it is desirable to ascertain the normal variations. It should always be borne in mind that a perfect form of blood-pressure apparatus has not, as yet, been devised, and that our readings are only approximately correct (*i. e.*, perhaps within 5 mm., if proper apparatus and technic are used). Numerous attempts have been made to establish in a statistical way what may be regarded as blood-pressures within the range of "normal." These data have been gathered from "wholesale" examinations of school children and college students (Lee, Barach and Marks, Judson and Nicholson, Alvarez, 8737 cases, etc.), accepted candidates for life insurance (Woley, 1000 cases; Fisher, 12,647 cases; Mackenzie, 31,934 cases; Symonds, 150,419 cases), army and navy recruits (Smith, Sorapure), candidates for athletic events, etc. (for literature, *cf.* Alvarez and Norris). A tabulated summary of some of these results is given on page 360.

As a result of such studies, we may say that with a wide cuff the normal ranges of systolic pressure by palpation are from 100 to 125 mm. Hg., while with auscultation and oscillatory methods they may be from 5 to 15 mm. higher. A somewhat higher pressure (10 mm.) may be expected after middle life. Janeway regarded a persistent pressure above 135 in the young or 145 after middle age as suspicious, and life insurance statistics indicate that the mortality in individuals with pressures above 150 is 35 per cent greater (Fisher). The pressures in women are usually somewhat lower and less variable than in men. This is illustrated in the recent statistical analysis of Alvarez, who found the arithmetical mean for women between the ages of sixteen to forty to be 115 mm., the extreme variations ranging from 85 to 155 mm. Similarly, the average pressures for men were found to be 126.5 mm., with variations ranging from 90 to 175 mm. Alvarez concludes from this extensive study that systolic pressures over 140 for men and 130 for women should be considered abnormal. During fifteen years that the writer has checked the pressures taken by students in the physiological laboratory, the systolic pressure was rarely found to vary beyond these limits. The highest normal limit for diastolic pressure found is 100, although pressures of 70 to 80 mm. are common. This gives a *pulse pressure,* as the difference between systolic and diastolic pressure is called, which varies from 35 to 50 mm. Various attempts have been made to establish rules as regards average blood-pressure at different ages. Thus, the suggestions have been made to add to the figure of 100 the age of the individual, or again to consider 120 the normal pressure at twenty years of age and to add 1 mm. for each additional two years (Faught). Even a casual perusal of statistics will convince anyone, however, that such

THE SYSTOLIC BLOOD-PRESSURE ACCORDING TO AGE OF DIFFERENT RACES BY VARIOUS OBSERVERS. (AFTER CADBURY.)

Age.	Wolfensohn-Kriss.	Fisher.	Katzenberger and several observers.	Judson and Nicholson.	Faught.	Alvarez.	Hunter.	Willits.	Faber and James.	McCay (*Bengali*).	Musgrave and Sison (*Filipinos*).	Chamberlain (*white men in Philippines*).	Chamberlain (*Filipinos*).	Concepción and Bulatao (*Filipinos*).	Trimble (*Chinese*).	Whyte (*Chinese*).	Cadbury (*Cantonese*).	Symonds.	Burlage (*women*).
6....	...	...	95	93.8	80–100	...	...	...	94.5										
7....	90	...	103	87.9	...	...	...	...	97.3	...	...	...	...	...	...	...	65		
8....	...	...	99	93.0	...	...	...	...	99.2	...	...	...	...	...	...	...	80		
9....	90	...	97	91.7	90–105	...	...	...	100.9	...	...	...	...	...	...	...	84	...	104
10....	...	...	104	99.0	...	...	...	...	102.4	...	...	...	...	...	...	...	80		
11....	98	...	107	95.8	...	...	...	...	104.1	...	...	...	...	...	...	...	83		
12....	...	...	108	99.9	95–100	...	...	...	105.9	...	...	...	...	...	...	...	88		
13....	99	...	114	104.0	...	...	...	...	107.6	...	...	...	...	...	...	...	89		
14....	...	...	...	105.8	...	...	...	...	110.0	...	...	...	...	...	...	...	97	...	124
15....	101	...	...	99.6	99–115	...	...	...	112.2	...	...	...	...	...	...	99	97	123.5	124
16....	...	...	...	...	...	126	...	...	115.3	...	...	...	...	...	...	104	100	123.5	
17....	113	118	...	...	95–120	128	120	...	...	...	...	...	...	...	...	104	100	123.5	
18....	...	...	...	...	...	127	...	120	...	...	...	...	112.8	110.7	...	108	102	123.5	110
19....	...	...	...	...	...	126	...	...	...	...	...	115.0	...	...	97	116	105	123.5	
20....	...	...	...	...	...	126	...	...	...	...	...	...	...	...	...	111	103	124.2	
21....	...	...	...	...	...	125	...	...	...	...	...	...	...	...	...	113	102	124.2	
22....	...	123.5	...	...	...	126	122	...	...	90–105	...	...	...	...	...	122	108	124.2	
23....	...	...	...	...	...	126	...	123	...	...	...	114.3	115.4	...	...	...	93	124.2	
24....	...	...	...	...	...	130	...	...	...	...	...	...	...	...	...	130*	103	124.2	
25....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	130*	100	124.5	
26....	...	...	...	...	...	126	...	...	...	...	...	...	...	111.9	90	...	95*	124.5	110
27....	...	125.6	...	...	...	...	123	...	...	...	...	115.9	...	...	...	...	110*	124.5	
28....	...	...	...	...	...	...	...	124	...	...	...	...	117.0	...	...	...	...	124.5	
29....	...	...	...	...	...	126	...	...	...	...	...	...	...	...	...	...	95*	124.5	
30....	...	...	...	...	...	...	...	...	...	...	108	...	...	...	...	...	105*	125.1	
31....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	130*	125.1	
32....	...	125.5	...	...	...	...	124	...	...	...	...	116.7	...	...	...	...	...	125.1	
33....	...	...	...	...	...	126	...	124	...	...	...	...	116.9	118.8	101	...	...	125.1	
34....	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	125.1	

* Only 1 case for this age was reported.

refinements are probably superfluous, as the observed variation at any age may agree with both the highest and lowest values so calculated for all ages.

Aside from sex and age, blood-pressure readings are apparently directly related to stature, weight and race. Thus, statistical studies show that both in men and women there is a difference of about 10 mm. between heavy-weight and light-weight individuals of the same height and age (Burlage, Symonds, etc.). As regards racial factors, recent observations indicate that the systolic blood-pressures of native Occidental races is uniformly from 10 to 30 mm. lower than in Caucasian races of Europe and North America (*cf.* table compiled after Cadbury, page 360).

Blood-pressures in Children.—Only a few of the statistical observations of the blood-pressures in children can be mentioned. According to Seitz and Becker, blood-pressure at birth averages between 75 mm. systolic and 45 mm. diastolic, and rises somewhat during the first few days. Leitao reports upon 200 infants less than a year of age as follows:

Age.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
2 months	68	50	18
3 "	78	50	28
7 to 8 "	78–84	54–60	20–34

A comprehensive study of older children together, with a review of previous studies, is given by Judson and Nicholson, who utilized the auscultatory method checked by the Erlanger apparatus, using oscillatory criteria. Their examination, based upon 2300 well-nourished children between the ages of three to fifteen, is given in the following table:

BLOOD-PRESSURE IN CHILDREN. (After Judson and Nicholson.)

Age, years.	Cuff width, cm.	Systolic pressure, mm. Hg.	Diastolic pressure (muffling of sound).	Disappearance.	Pulse pressure.
3	9	92.0	58.4	41.6	33.6
4	9	92.6	61.7	49.1	30.9
5	9	91.6	60.0	46.0	31.6
6	9	93.8	63.5	59.9	30.3
7	9	87.9	64.2	49.2	22.7
8	13	93.0	59.6	41.0	33.4
9	13	91.7	62.2	50.0	29.5
10	13	99.0	64.0	47.3	34.4
11	13	95.8	62.3	49.1	33.5
12	13	99.9	59.6	37.6	40.3
13	13	104.0	63.2	47.0	30.8
14	13	105.8	63.7	48.2	42.1
15	13	99.6	61.8	43.6	37.7

The following general conclusions may be drawn from these and other studies:

1. Systolic pressure gradually increases during childhood, ranging from 75 to 90 mm. during infancy, from 90 to 110 mm. during childhood and from 100 to 120 mm. toward puberty.

2. The diastolic pressure averages around 50 mm. during the first few years of life and thereafter, and until puberty remains relatively constant at 60 mm.

3. As a result of the progressive increase in systolic pressure with a constant diastolic pressure, the pulse pressures increase from 18 to 20 mm. during the first year to over 30 mm. by the third year, reaching adult variation after the tenth year. A study of blood-pressures in girls during adolescence has recently been reported by Burlage (*cf.* table, page 360). There appears to be a general increase in systolic pressure from 104 mm. at nine years of age to about 124 mm. at fourteen and fifteen years. The systolic pressure then gradually declines until between eighteen and twenty-six years it remains fairly constant at 110 mm. The diastolic pressures were found to rise from 63 mm. at nine years to about 76 mm. at fourteen years, remaining constant during the following years.

Blood-pressure in Old Age.—While the blood-pressure has a tendency to increase after forty-five or fifty years of age, owing to possible arteriosclerotic changes, statistical studies in the very old indicate that there is a tendency for it to again reduce after the age of sixty-five (Wildt, Bores). This is indicated in the following tabular summary:

THE BLOOD-PRESSURE OF WOMEN. (After Norris.)

Age, years.	Number examined.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
65 to 69	21	154	83	71
70 to 74	29	158	83	72
75 to 79	24	170	88	81
80 to 84	16	183	85	91
85 to 89	7	170	90	77
90 to 94	3	137	80	53

THE BLOOD-PRESSURE OF MEN. (After Norris.)

Age, years.	Number examined.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
65 to 69	11	145	81	63
70 to 74	10	166	91	75
75 to 79	14	159	89	77
80 to 84	11	163	84	80
85 to 89	0			
90 to 94	4	145	81	65

Significance of Hypotension and Hypertension.—According to dynamic laws, every alteration in the rate and output of the heart, as well as every variation in the caliber of the peripheral arterioles, must be accompanied by an alteration in pressures. Such, however, is not

the case in the body. Under normal conditions the blood-pressures remain quite constant. This is made possible through a well-balanced compensatory mechanism. If arterial pressures have a tendency to rise, due to vasoconstriction, reflexes are set up from the large vessels which slow the heart, reducing its minute output and tending to restore the pressure relations to normal. If the heart accelerates and increases its discharge, as it does during exercise, thereby tending to increase the systolic and diastolic pressures, a reflex dilatation of the arterioles is induced which tends to restore pressure relations practically to their normal level again. In these and similar ways, the compensatory mechanisms are adapted to prevent great fluctuations in arterial pressures (*cf.* page 143). When the pressure relations are decidedly high or low, therefore, we are warranted in assuming that some circulatory derangement, usually of a morphological nature, exists which prevents the operation of these normal regulatory mechanisms.

Practically, the measurement of blood-pressure is used to determine whether the pressure is permanently high or low. The conditions giving rise to permanent hypertension and hypotension are discussed in detail in other sections, but may be here classified for convenience after the plan of Janeway:

Hypertension:
1. *Functional:*
   - (*a*) Physiological (*i. e.*, due to excitement, exertion, labor, pain reflexes, etc.).
   - (*b*) Toxic (as morphine, lead and nicotine poisonings, gout, uremia and rheumatic affections).
   - (*c*) Cerebral anemia and asphyxia.
2. *Essential* (*i. e.*, accompanied by organic change or indicating derangement of regulating power):
   - (*a*) Arteriosclerosis.
   - (*b*) Nephritis.
   - (*c*) Due to unknown causes and associated with no discernible alteration (hyperpiesis).

Hypotension:
1. *Functional:*
   - (*a*) Diarrhea, excessive sweating, etc.
   - (*b*) Hemorrhage.
   - (*c*) Shock.
   - (*d*) Acute infections (except meningitis).
2. *Essential:*
   - (*a*) Cachectic (in tuberculosis, carcinoma, general paralysis).
   - (*b*) Enteroptotic (relaxed abdominal walls, enteroptosis of varying degree).

The etiology of high blood-pressure and its relation to pathological changes in bloodvessels, heart and kidney has been frequently discussed.[1] Three types of cases apparently exist:

1. High blood-pressure without discoverable cardiac, renal or arterial involvement, the so-called *hyperpiesia* of Allbutt. The cause of the high blood-pressure remains unknown. The circulatory volume is not in excess. The increased resistance is usually located in the smaller arterioles (hypertonus) or in the capillary stream bed.

2. High blood-pressure associated with arteriosclerosis and with cardiac and renal manifestations.

3. High blood-pressures secondary to chronic nephritis.

Rhythmic Variations of Blood-pressure.—In establishing a certain figure for systolic and diastolic pressures in man, it should be borne in mind that these figures represent only approximately the highest and lowest pressures in the artery. This is due, in the first instance, to the fact that the intra-arterial systolic and diastolic pressures vary with rhythmic changes in the heart cycle and with the acts of respiration. These variations are of such a nature that in the majority of normal individuals both pressures are lower in inspiration than during expiration. The variations of systolic pressure are often great enough to be detected by different criteria. Thus, if the pressure is allowed to fall slowly and auscultation is carefully carried out, it is often found that the sound is first limited to the expiratory beats, while, after the pressure has fallen 3 to 5 mm. more, a sound is present for every beat. Similarly, in the Erlanger tracing, the supported wave in the descending limb often occurs at first on one of two waves of a respiratory group before it becomes mounted on all waves. In these ways we may estimate the highest and lowest systolic pressures.

While these variations of normal pressure are not of extreme importance, a determination of the highest and lowest systolic pressures may be of great diagnostic significance. Thus, it happens that pericardial adhesions or tumors may be so situated that they exert a traction or compression upon the heart or large vessels during one respiratory phase. The difference between inspiratory and expiratory pressures may then be so great as to be of diagnostic value.

[1] For a comprehensive discussion of "clinical hypertension" the reader is referred to Allbutt (Diseases of the Arteries, etc., London, 1915) and Christian and Mackenzie (Oxford System of Medicine, London, 1920). The following recent articles deal with present-day aspects of the question and contain an extensive bibliography: Barach (Jour. Am. Med. Assn., 1922, **79**, 2140), Barnes (New York Med. Jour., 1922, **115**, 73), Christian (New York Med. Jour., 1921, **21**, 292; Wisconsin Med. Jour., 1922, **20**, 455), Elliott (Jour. Am. Med. Assn., 1921, **76**, 1467), Hewlett (Med. and Chir. Bull., 1912, **4**, 211), Hopkins (Am. Jour. Med. Sci., 1919, **157**, 826), Kisch (Med. Klinik., 1922, **18**, 691), Mosenthal (Med. Clinics, North America, 1922, **5**, 1139), Moschcowitz (Jour. Am. Med. Assn., 1921, **77**, 1075 and 1922, **79**, 1196; Am. Jour. Med. Sci., 1919, **158**, 668), Orr and Innes (Brit. Jour. Exp. Path., 1922, **3**, 61), Riesman (Jour. Am. Med. Assn., 1919, **73**, 330) and Ringer (Am. Jour. Med. Sci., 1921, **161**, 798).

Blood-pressure in Extreme Cardiac Irregularity.—When the heart is markedly irregular or the auricles are fibrillating, the pressure varies considerably during consecutive beats; in fact, some beats may entirely fail to reach the instrument, thus showing a pulse deficit. To determine systolic and diastolic pressures is often impossible with the available criteria. Some idea of the systolic pressures may be obtained in such cases by estimating the "average systolic pressure" according to the procedure suggested by James and Hart: The pressure in the cuff is raised until all pulsations are obliterated. It is then lowered 10 mm. at a time and each time the number of pulse beats that pass peripheral to the cuff are counted. An assistant counts the apex beats at the same time. The average systolic pressure is then obtained by multiplying each different pressure tested by the number of beats passing per minute. These products are added and the sum divided by the number of apex beats per minute. The quotient gives the *average systolic pressure.*

FIG. 126.—Sphygmomanometer tracing from case of auricular fibrillation, showing irregularity in amplitude of consecutive oscillations and the difficulty of determining either systolic or diastolic pressure by the oscillatory method.

A simpler and, in some respects, a preferable method, which the author employs, consists in writing the highest and lowest systolic and the highest and lowest diastolic pressures, the pulse having first been counted: The cuff is inflated until the pulse is obliterated. Upon gradually deflating the system of air, the pressure is noted when the first sound is heard peripheral to the bag. This is the highest systolic pressure. The pressure is then released until the sounds for all waves are audible. This is the lowest systolic pressure. The estimation of any diastolic pressure is, however, very unsatisfactory. The oscillation method is of less value in these cases, for the theory of this criterion presupposes that the pulse pressure remains at least approximately constant or varies rhythmically, as during natural respiration. It is, however, possible to obtain an approximate idea in many cases when groups of waves remain per-

manently smaller. There would be little question, for example, that the diastolic pressure was approximately 85 in the record shown in Fig. 126. At about the same level, the sounds of most of the beats disappeared on auscultation.

The Value and Limitations of Pulse-pressure Determinations in Disease. —Blood-pressure determinations are sometimes employed to follow the changes in the circulation during disease processes or to test the effect of medication, it being sought not only to determine whether the circulation is changed but also what part is at fault. In this capacity, it has been used largely in the acute febrile affections and in chronic valvular lesions. In neither group have the pressure determinations given the results anticipated; partly, no doubt, because the readings have not been taken at sufficiently close intervals and partly because the systolic and diastolic pressures and their differences, the pulse pressures, were not studied in relation to the heart rate. If information concerning the changes in the circulation is desired, it is just as important to take hourly readings of pressures as it is to make the temperature and pulse-rate charts.

We may first of all inquire what information the pulse pressure gives us concerning the systolic discharge of the heart. The pulse pressure is an index of the volume of cardiac discharge only when it may be assumed that neither the viscosity of the blood, nor the diameter of the peripheral vessels nor the cubic increase in volume for definite pressure increments varies. It may, therefore, be set down at once that pulse pressure cannot be an exact measure of the systolic discharge, and the only question of interest is whether, recognizing its limitations, it may be a sufficiently exact criterion. The experimental investigation (Dawson and Gordon, Henderson, Wiggers) indicates that, although there is a general correspondence between the amplitude of pulse pressure and the output of the heart—in the sense that both increase and decrease synchronously so that the course of one may be prophesied from the other—there is no quantitative relation. The same pulse pressure may at different times correspond to systolic discharges of very different volumes. Unless subsequent reinvestigation, by more accurate methods, should speak to the contrary, the clinician is not warranted in assuming that, because the pulse pressure is equal to one obtained some days or weeks previous, therefore, the output of the heart has not altered; or, because the pulse pressure does vary, that the output has necessarily changed. The pulse pressure is not a quantitative measure of systolic output, *but when compared to some not too remotely preceding observation in the same individual* it may be used as an indication of the direction in which the discharge varies. Thus, by following the pulse pressure during periods of an acute febrile process or during the presence of a valvular lesion or a myocarditis hour by hour, one may obtain valuable information as to whether the output is improv-

ing or deteriorating, and this, as indicated by experimental investigations, occurs in spite of considerable variation in viscosity or peripheral resistance.

One is not warranted in assuming any correspondence whatever between pulse pressure and systolic output in different individuals in whom the viscosity of the blood, the volume and the vascular elasticity and tonicity are different by an unknown amount due to some diseased condition, such as arteriosclerosis, infections, cardiac disease, etc.

Investigators have established that the systolic output is directly dependent on the heart rate, and in such a way that an increase in rate tends to decrease the output per beat. This may frequently be indicated by studying the product of the heart rate and pulse pressure. Under normal conditions this product tends to remain constant (Erlanger and Hooker) or, if any change occurs, the tendency is toward an increase as the heart accelerates. When the output of the heart is primarily affected, as in hemorrhage and shock through a reduction of its blood supply, or by a diminution in its contraction amplitude, as occurs in depressing toxic action or in valvular insufficiency, the product decreases. It is obviously possible, however, that even when hourly estimations of pulse pressure are made that their comparison with preceding observations may be erroneous when considerable variation in the tonus of the peripheral vessels, the viscosity of the blood or the total blood volume occurs. Recently, Skelton has again tested the general proposition that the product of pulse pressure and heart rate gives an index of the minute volume discharged by a perfused heart and finding no proportional relations between the two, concludes: "That the product of pulse pressure by pulse rate is of no value as a measure of cardiac output." Actually, these results merely confirm what has been generally admitted and emphasized, viz, that no quantitative relations exist. A perusal of the tables shows equally clearly, however, that *without fail* the product of pulse pressure and heart rate changes in the same direction as the minute discharge.

In order to decide whether the output of the heart or the peripheral resistance or viscosity is the chief variable, a comparison of the pulse pressure with the height of systolic and diastolic pressures has been suggested. Erlanger and Hooker have constructed the following table as indicating the relations:

Diastolic pressure.	Determinable factors. Pulse pressure × pulse rate.	Causative factors. Energy from heart.	Causative factors. Peripheral resistance.
Constant	Increased	Increased	Diminished
	Diminished	Diminished	Increased
Increased	Unchanged	Increased	Increased
	Increased	Increased	Unchanged
	Diminished	Unchanged	Increased
Diminished	Unchanged	Diminished	Diminished
	Increased	Unchanged	Diminished
	Diminished	Diminished	Unchanged

It is evident that, in general, a decrease in the product of the heart rate and pulse pressure indicates that the heart output is unchanged when it is accompanied by an increased diastolic pressure; but that an increased product likewise indicates an unchanged output when the diastolic pressure is diminished. The practical value of such a guiding table has been frequently questioned. Thus, Norris points out, as an example, that, in nephritic hypertension, both an increase in diastolic pressure and in the product occur, which would be interpreted as due to an increased cardiac output and an unaltered peripheral resistance—a conclusion evidently erroneous. This, however, should be cited *not* as an example of *a defect in the table, but of its misapplication;* for, as variations in the pulse pressure can reasonably be expected to be of prognostic value only when compared *in the same individual with observations preceding at not too distant intervals, so this table is restricted in its applicability to consecutive observations in the same case.*

A similar though less accurate procedure has been evolved by Strasburger, who compared the relation between pulse pressure and systolic pressure as a quotient (blood-pressure quotient) $-\ B.P.Q. = \dfrac{\text{Pulse pressure}}{\text{Systolic pressure}}$. This formula is less reliable than that offered by Erlanger and Hooker, partly because the maximal pressure follows the mean pressure less accurately than does the diastolic, but chiefly because it contains no factor allowing for heart-rate variation.

It may be pointed out, in conclusion, that this most promising field, say hourly or two-hourly determinations of pulse pressures and heart rates during infectious disease or critical stages of cardiovascular lesions has not been adequately invaded. Clinicians have too often been content with occasional and haphazard determinations which have yielded results of no importance and, hence, can probably be dispensed with entirely. Whether the efficiency of the circulation is improving or whether failure is threatened can only be determined by frequent and systematic studies of pulse pressure and heart rate.

A number of so-called "functional tests" of the circulation, which are based upon consideration of combined heart-rate and blood-pressure changes during postural changes (Crampton, Barach and Marks and others), or during exercise of a more or less graded form (Graupner, Barringer), have been developed in the hope that they may give more definite evidence than is otherwise obtainable of the ability of the heart mechanism to act reciprocally in adapting the circulation to tissue needs. For details the original articles as appended in the bibliography should be consulted. While all of these tests are the outcome of earnest attempts to apply known dynamic principles of the circulation to the solution of difficult practical problems, it must

be admitted that each one involves so many unknown or undeterminable factors that considerable hazard exists in attaching significance to the results until such time as their accuracy shall have been demonstrated by the experimental method on animals, which to this time has not been attempted, and for very excellent technical reasons.

Methods Designed to Estimate the Mechanical Energy or Work of the Heart.—Two attempts have been made to estimate the mechanical energy of cardiac action by procedures related to blood-pressure determinations, viz., by the application of the sphygmobolometer or sphygmobolograph of Sahli and the energometer of Christen.

The theory upon which these measurements are founded is briefly as follows: During every cardiac systole a certain amount of mechanical energy is liberated. About 1 per cent is utilized in moving the blood onward (kinetic energy), the rest is transformed to elastic tension of the wall (potential energy). The energy utilized in filling and expanding the arteries, and so creating the entire pulse wave (pulse energy), is not directly measurable. It is possible, however, that the energy required to produce the pulse in a limited area of artery (pulse impact energy) can be estimated, and the methods rest upon the assumption that this gives information concerning pulse energy.

The Sahli Sphygmobolograph.—Sahli attempts to estimate the energy of the pulse impact by the product of the distance that the wall expands and the compressing force. His sphygmobolometer first devised for this purpose is probably less exact and more difficult of application than the sphygmobolographic method. The sphygmobolograph is essentially a Jaquet sphygmograph (new model), in which the two tiny rollers usually pressing the paper against the propelling roller actuated by clockwork have been replaced by nine tiny rollers which write a series of abscissæ lines upon the paper as it passes. These rollers are not equidistant, but so placed that the distances between them represent a movement of 0.05 mm. In this way the excursion of the arterial wall can be estimated from the pulse tracing. The pressure exerted by the spring is determined by reading the number on the dial and, by reference to an accompanying table, the pressure can be estimated in grams.

It is apparent that a single computation at any one pressure is not sufficient, since every different tension will yield a different product. The product is, therefore, determined during the entire gamut of pressures. The largest product is chosen as a standard for comparing the energy of pulse waves of different individuals and of the same individual at different times.

Leaving the question as to the accuracy of the principle out of consideration, the method is at best a crude one in consideration of the limitations of the Jaquet sphygmograph. How correctly the

gram readings on the instrument correspond to the pressure exerted on the vessel wall depends on its adjustment. How truly the amplitude of the button movement in this instrument, which has an inadequate vibration frequency, corresponds to the actual movement of the artery depends largely upon the vigor of the pulse beat. Finally, how accurately the movement of the button under pressure is an index of the energy exerted by the entire pulse wave is determined by the elasticity and tonus of the radial under the button.

Energometer Method.—In some respects the energometer method of Christen is an improvement. This apparatus is shown in Fig. 127. Its cuff is applied to the arm or thigh and brought to the proper

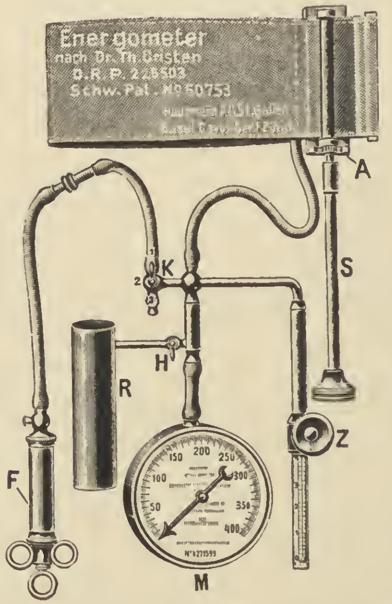


FIG. 127.—The energometer. (After Christen.)

tension by tightening the key, *S*. The position of the volume syringe is placed at zero by means of the screw, *Z*, and stop-cock, *H*, is closed. Air is then pumped into the system by the pump, *F*, and the stop-cock, *K*, is closed. The mean pressure is read either in terms of centimeters of water pressure or in millimeters of atmospheric pressure at the mid-point of the oscillations of the spring manometer, which, according to Christen, has an inherent vibration frequency of 20 per second. If the oscillations are too large the sensitiveness is diminished by increasing the capacity of the system by opening the stop-cock, *H*, and so adding the reserve space, *R*, to the system. The piston of the volume pump is now moved in by

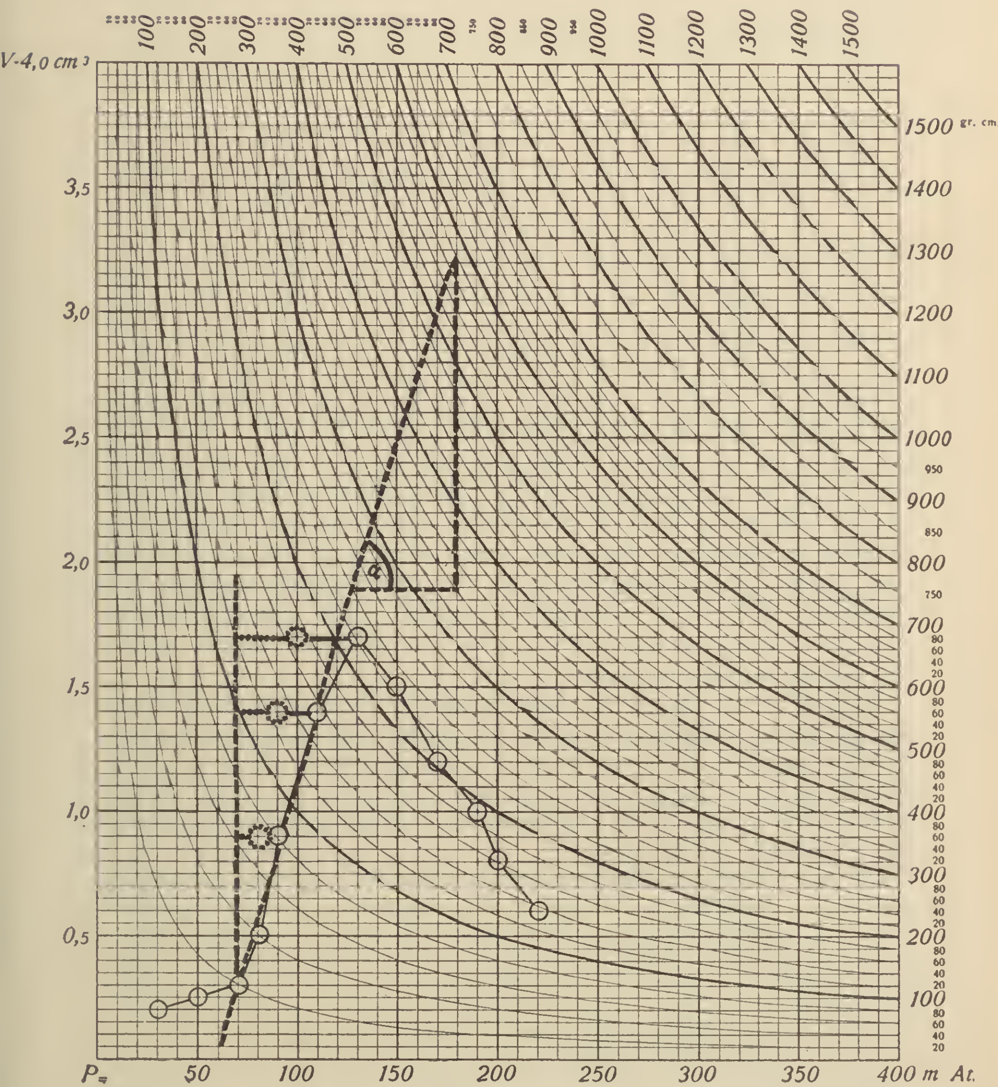


FIG. 128.—Dynamic diagram. Discussion in text. (After Christen.)

the screw, Z, so that the pressure before read at the upper excursion now becomes the lower pressure. The volume is then read off. The product of the mean pressure and volume change is expressed in gram centimeters, as shown in the following table:

Pressure.	Volume.	Pressure × volume = energy of pulse impact.
30	0.2	6.0
50	0.25	12.5
70	0.3	21.0
80	0.5	40.0
190	0.9	81.0
110	1.4	154.0
130	1.7	221.0
150	1.5	225.0
170	1.2	204.0
190	1.0	190.0
200	0.8	160.0
220	0.6	132.0

The largest product is evidently equal to 225 gm. cm. To obviate calculations, Christen has constructed a hyperbolic scheme (Fig. 128). By laying off the volume reading on the abscissæ and the pressure reading on the intersecting ordinates, the product is found by following the hyperbolic curve to the right or upper margin. The product so obtained represents the *gross energy of the pulse impact, i. e.,* the sum of the energy contributed by the pulse impact and the wall elasticity. $P. V. = A + A'$, in which P = the pressure change, V = the volume change, A = energy of the pulse impact and A the energy of the elastic wall.

The *net energy*, due to the impact, can be determined by subtracting the latter. The net value can be ascertained from the diagrams by drawing back horizontal lines to the point where the bend in the ascending curve occurs and taking a point (heavy circle) in the middle of this line. The hyperbole upon which this falls represents the net energy of the pulse.

For the limited clinical application, Christen's original monograph should be consulted. Criticism or commendation must be tentatively withheld until its possibilities can be further tested out.

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CHAPTER XVIII.

THE VOLUME FLOW—VENOUS AND CAPILLARY PRESSURES IN MAN.

By *volume flow*, is understood the quantity of blood flowing through an organ or the entire body in unit time. It is to be distinguished from the *velocity* of the blood flow, which means the rate at which blood moves in unit time. The latter depends upon the diameter of the tube as well as upon the volume flow; hence, one may be altered without the other. This distinction, which is not always made, is of more than academic interest. The important question is often raised whether the circulation functionates in such a way that an adequate *volume of blood*—upon which a proper interchange of waste products, nourishment, etc., depend—is passing through the organs. It is of less concern whether it flows through the narrow arteries at a great velocity or through large arteries at a lesser velocity, provided only that the supply is sufficient. We shall, therefore, concern ourselves only with the question of volume flow and refer back to the question of velocity to chapters in the first section.

METHODS OF ESTABLISHING THE VOLUME FLOW.

Plethysmographic Method.—This method depends on the principle demonstrated by Brodie that if the vein from an organ is suddenly occluded the volume increases constantly for a short interval before venous congestion has occurred. In the plethysmographic methods (Müller, Hewlett and Van Zwaluwenburg) (Fig. 129) the forearm is placed in a plethysmograph, *P*, connected with a sensitive manometer and float (Müller) or with some form of volume recorder, *V* (Hewlett and Van Zwaluwenburg). A narrow pressure cuff, *C*, such as is used in determining blood-pressure, is placed around the arm above the plethysmograph, with the lever of the volume recorder writing horizontally on a revolving drum. The pressure in the cuff is raised quickly to about 50 mm. of mercury by opening a stop-cock communicating with a large flask, *A*, containing air under such pressure. This pressure is sufficient to prevent venous outflow but presumably does not affect arterial inflow. For a short time the arm swells at a constant rate, but soon diminishes because blood is dammed up in the capillaries, and later still, when the venous pressure has risen

extensively, blood is forced out under the cuff. Only the first part of the curve can, therefore, be used to determine the normal arm flow. By subsequently closing off the plethysmograph, Z, and allowing a definite quantity of water to flow from the burette, Y, into the flask, the lever record can be calibrated and the quantity of blood flowing into the arm calculated. By simultaneously recording the time in seconds, the flow per second is determined. The volume of the forearm enclosed within the plethysmograph is ascertained by determining the volume of water displaced by thrusting it into a vessel of water to the same mark at which it entered the plethysmograph. The flow may then be calculated in terms of cubic centimeters per minute per 100 gm. arm substance.[1]

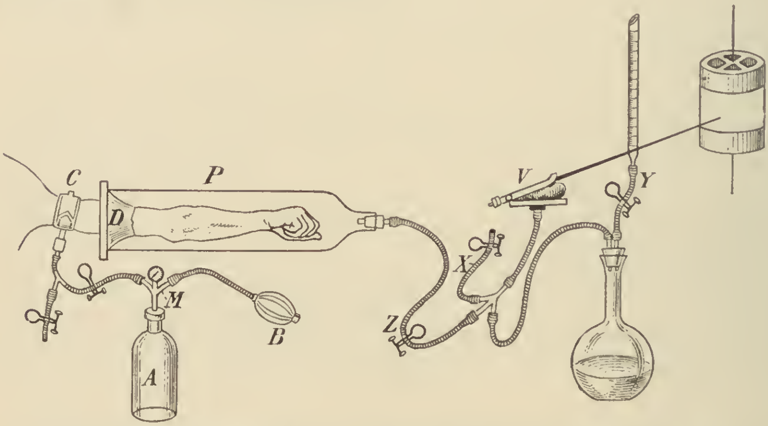

Fig. 129.—Diagram showing Hewlett and Van Zwaluwenburg's method for estimating the rate of blood flow in the arm. (After Hewlett and Van Zwaluwenburg.)

Calorimetric Method.—This method, devised by Stewart, depends upon the principle that the heat given off by the hand at rest is derived almost entirely from the circulating blood. Knowing the temperature of the arterial blood, the temperature of venous blood and the number of calories given off in a given time, the amount of blood that must have flowed in a given area can be calculated by the following formula:

$$Q = \frac{H}{T - T''} \times \frac{1}{s}$$

In this formula, Q is the blood volume; H, the heat eliminated (in calories); T, the temperature of arterial blood; T', the temperature of venous blood; and s is the specific heat of blood which equals 0.9. The volume of the hand is determined as before by measuring the amount of water displaced.

[1] By substituting a segment capsule as a volume recorder, Hewlett and Van Zwaluwenburg have calculated accurately *the pulse flow, i. e.*, the arm flow during each pulse beat.

The calorimeter, into which either a hand or foot is placed, consists of an interior copper vessel containing a known amount of water. Into this the hand is inserted through an opening in the lid, heat-tight closure being obtained by a collar of felt. The interior vessel is packed in cork to prevent loss of heat or irregular cooling when exposed to draughts. The heat lost by the calorimeter is estimated separately and added to the results of experiments. Previous to an experiment, the hand is immersed in water at the temperature of the calorimeter for ten minutes. The temperature within the calorimeter is read to hundredths of a degree.

The temperature of the incoming arterial blood is considered to be 0.5° lower than rectal temperature, that of the incoming venous blood as equal to the average temperature of the calorimeter during an experiment.

It may be pointed out that both of these methods, which measure the volume flow through a peripheral organ, do not necessarily give an indication of a similar flow through other organs, since it is well known that in many conditions a sort of reciprocal relation exists between the splanchnic and limb circulation.

Gasometric Method.—The gasometric methods attempt to estimate the volume flow of the entire circulation, or the *minute volume*, as it is termed. If we count the pulse rate as well, the average volume of blood flowing through the peripheral vessels during the interval of a single pulse beat, that is, the *pulse volume*, may be determined. Although the method is somewhat complicated and ill-adapted for ordinary clinical usage, the results obtained with it are of such great importance that a brief description of the essential principles and processes may be given.

One method is based upon the principle first enunciated by Fick, in 1870, that if we know how much oxygen is consumed by the tissues per minute and how much oxygen is required to arteriolize, say 100 cc of venous blood, we can calculate the blood flow required to deliver this quantity of oxygen to the tissues. The amount of oxygen consumed may be determined by measuring the quantity taken from the air in a minute. The volume of oxygen necessary to convert venous into arterial blood is determined by taking the difference between the volume per cent of oxygen in the venous and in the arterial blood. Then the following proportion can be made:

$$\text{Minute volume} : \text{oxygen used} = 100 : \begin{array}{c}\text{volume per cent difference between}\\ \text{arterial and venous blood.}\end{array}$$

Thus, if the oxygen content of arterial blood is 20 volume per cent, that of venous blood 13 volume per cent, the difference will be 7 volume per cent. If now 200 cc of oxygen were used during that minute:

$$\text{Minute volume} = \frac{200 \times 100}{7} = 2857 \text{ cc.}$$

If this is divided by the number of heart beats, for example, 70 per minute, the pulse volume of 40.8 is found.

Application in Man.—In order to apply this principle, it is evidently necessary to know:

(*a*) The volume per cent of oxygen of the arterial blood as it leaves the heart.

(*b*) The volume per cent of oxygen of the venous blood in the right heart.

(*c*) The volume of oxygen consumed per minute.

To determine the volume per cent of oxygen in the arterial and venous bloods, it is obviously impossible in man to make direct blood-gas analyses as in animals. It is, therefore, necessary to utilize indirect methods.

Loewy and Schrötter made the first attempt at determining venous and arterial gases in man. They attempted to measure the gases of the venous blood by blocking a lobe of the right lung by means of a catheter and balloon and allowing alveolar air and venous blood to come into equilibrium. From the partial pressure so obtained, they calculated the percentage of oxygen in venous blood. By calculations, taking into account the dead space, they determined the gaseous tension of arterial blood from an analysis of expired air. The introduction of the pulmonary catheter is beset with so many unpleasant effects, however, that neither the respiratory nor circulatory functions may be regarded as entirely normal.

The method of Plesch obviates these difficulties incident to the determination of venous gases and is carried out in the following manner: The subject, after a preliminary deep expiration, breathes into a bag of nitrogen during two respirations, then, by quickly turning the stop-cock, breathes for five to fifteen seconds into an empty bag of 3 liters' capacity. Having determined the composition of this rebreathed air, the tension of oxygen in venous blood is calculated by multiplying the percentage volume by the existing barometric pressure corrected for aqueous vapor tension at 37° C. The percentage oxygen saturation of the blood is estimated by the use of a dissociation curve. By following the line corresponding to the oxygen tension up until it strikes the curve of CO_2 tension (as found in alveolar air) and reading the figure of this abscissa on the left-hand side, the percentage of oxygen saturation can be determined for venous blood. The volume per cent of oxygen in venous blood may then be determined by multiplying this figure by the oxygen capacity of that individual. The oxygen content of arterial blood is usually determined by the well-known method of Haldane and Priestley, in which, after a normal inspiration, a deep expiration is made through a tube, and a sample of the last portion is analyzed.

The chief objections to the procedure as performed are that the

O_2 dissociation curve of hemoglobin is not constant for different individuals and varies, moreover, with changes in the CO_2 content of the blood. Consequently, it virtually becomes necessary to determine not only the O_2 but also the CO_2 tension and, in addition, the O_2 absorption curves of the blood at those pressures for every individual case. The earlier attempts to overcome these sources of error at first bore no fruit. (For discussion, *cf*. Liljestrand and Lindhard.) Considerable advance was made as regards the accuracy of blood-gas determination when it was found clinically feasible to obtain samples of arterial blood directly for analysis by puncturing the radial artery. The problem of determining the gaseous content of "mixed" venous blood as it returns to the heart still remained, however, especially as it was demonstrated that the volume per cent of O_2 and CO_2 varies greatly in veins coming from different regions of the body (Hill and Nabarro).

In 1914, Christiansen, Douglas and Haldane, however, described a new and improved method of determining the gas content of mixed venous blood and, in 1922, Douglas and Haldane extended these observations. In their methods, both lungs are used as an aërotonometer on Pflüger's principle, bringing both O_2 and CO_2 in the alveoli into equilibrium with venous blood. In brief, their method is as follows: The subject breathes a mixture of CO_2, O_2 and N of such proportions as correspond somewhat to anticipated partial pressures in the veins. After taking a maximum breath of this mixture and holding the breath for four seconds the subject exhales about half of this volume and, after another six seconds, the remainder. At each exhalation a sample is taken for analysis. When the CO_2 or O_2 content of the two samples agree fairly closely, we may assume that the partial pressures of the gases, alveolar air and venous blood are in equilibrium. Knowing the gas pressures of both arterial and venous blood, it is then possible, on the basis of corresponding dissociation curves, to calculate the volumes of CO_2 given off and O_2 absorbed.

A simple modification of this method, suggested by Henderson and Prince, has the advantage that the time of holding the breath is considerably reduced. This is accomplished by rebreathing the same air over at intervals of several minutes. The procedure, in brief, is as follows: The subject makes the deepest possible expiration into an empty bag. The bag is closed and the subject breathes normally while its contents are analyzed for CO_2. After a few minutes, the subject again inhales deeply from the bag and draws in the entire contents, and after holding it for ten to fifteen seconds, exhales it again. This is repeated until constant gas relations are found in subsequent analyses, at which time an equilibrium between

mixed venous blood and alveolar air may be assumed to exist.[1] Still another procedure, which avoids to a considerable degree the circulatory disturbances occasioned by these artificial modes of respiration, has also been described by Barcroft, Roughton and Shoji. Their method attempts, by a single estimation, to give the composition of mixed venous blood at any given moment of time: The subject takes a deep respiration followed by three or four normal respirations from a bag containing N and then exhales, a sample of the alveolar air being collected and analyzed. The partial pressure so determined and laid off on the oxygen dissociation curve gives the O_2 content of 1 cc of mixed venous blood.

Before these technical improvements taking into account not only technical errors but the maintenance of approximately normal circulatory conditions had been developed, other investigators sought to escape these difficulties by computing the minute volumes through the utilization of harmless gases not normally concerned in respiratory exchange. For this purpose, nitrous oxide was independently suggested and tried by Zuntz and Krogh and Lindhard. This method, which until recently has been the one favored by most investigators, has been extensively employed (Fridericia, Boothby, Lundsgaard, Liljestrand and Lindhard, etc.). The procedure is carried out as follows: The subject inhales a deep breath of a mixture of N_2O and O_2 from a spirometer or bag and, after holding the breath for a few seconds (to allow adequate mixture in the alveoli and to saturate the pulmonary tissue itself), he expires sufficiently to return the chest to a normal position of expiratory rest. A sample is taken. In this position, the breath is held for thirty seconds, after which a forcible expiratory effect is made and another sample obtained. From a diminution of the percentage of N_2O in the second sample and a knowledge of the volume of air kept in the lung after the first sample is taken (determined by the spirometer and the subjects' vital capacity), the volume of N_2O taken up in the thirty-second interval is determined. Knowing the absorption coefficient of N_2O in blood, the volume flow can be calculated. Thus, suppose 55 cc of N_2O is absorbed in thirty seconds and the percentage of N_2O is 11.08, then taking 0.405 as the absorption coefficient, the amount of blood required to absorb 55 cc of N_2O is $\frac{55}{0.405 \times 11.08} \times 100 =$ 1230 cc, or 2460 cc per minute. In a similar manner, the O_2 absorbed can readily be estimated. When this is done, however, it is usually found that the rate of O_2 absorption so determined is greater than its rate of absorption determined by respiratory experiments just previous to or just after the test. This has been interpreted as indi-

[1] *Cf.* also Henderson (Arch. neerland. de physiol., 1922, **7**, 378).

cating that a temporary increase in blood flow occurs through the lungs during the experiment and consequently a correction has been customary. This is done in such a way that the O_2 absorption determined during the experiment conforms to that obtaining with other methods.

This procedure is open to question. Thus, R. Tigerstedt points out that the mode of correction is based upon the assumption that the blood-volume flow through the lungs must be the same for every 100 cc of O_2 absorbed, *i. e.*, to say, that the minute volume is regarded as a specific function of the O_2 absorption. Upon calculating the blood-flow equivalents in Lundgaard's and Boothby's curves, Tigerstedt comes to the conclusion that this varies so markedly in different individuals, as well as at different times in the same individual, that the "reduced values" are subject to greater error than the originals. Furthermore, the method has been criticized on the ground that it is improbable that a sufficient mixture of air in the alveoli can be accomplished before the first sample is taken (Sonne, Douglas and Haldane).

The Roentgenographic Method.—If two instantaneous teleroentgenograms (*cf.* page 400) are taken respectively at the end of diastole and at the end of systole, and the surface areas of the silhouettes are determined by a planimeter than it is possible by the use of Bardeen's formula (Volume = $0.53\ H^{3}/_{2}$) (*cf.* page 403) to estimate both the systolic and diastolic volumes of the heart. The difference represents the systolic discharge. This method has been especially developed by Meek and Eyster, and their original communication should be consulted as to details (*cf.* bibliography at end of Chapters XVIII and XIX).

The Mass Movement and the Recoil Curve.—While the foregoing methods offer a means of determining the minute volume of the circulation and the systolic output of the ventricle, it gives no details of the mass movements and distribution of the blood during systole and diastole. This, Henderson has sought to do by recording the recoil curve of the body while the breath is held. To accomplish this, Y. Henderson devised the following apparatus: The subject lies on a horizontal board, which is suspended from a frame by four music wires and prevented from undergoing lateral movements by pointed steel pins resting in conical cups on the frame. The horizontal movements magnified one hundred times are recorded on a smoked surface.

The principle of the apparatus is briefly as follows: When a subject is supported on a swinging table, every mass movement of blood headward or feetward is associated with an equal movement of the body in an opposite direction. If a headward and feetward movement occur simultaneously, the movement of the body depends

upon their algebraic sum and the curve gives a record of the relative distribution of blood above and below the center of body gravity. Thus, during systole the algebraic mass movement occurs first headward to a slight degree, then markedly feetward and again markedly headward. The second, or feetward, movement occurs synchronously with the carotid rise, and has been interpreted as indicating the ejection of blood into the aorta. The last, or headward, movement is interpreted as due to the movement of blood beyond the arch of the aorta.

In order to obviate the difficulties due to (*a*) periodicity of the recording apparatus and (*b*) errors due to respiratory movements, Heald and Tucker have recently recorded the recoil curve of an individual standing on a suspended platform through the use of the "hot-wire" microphone connected to a string galvanometer. This apparatus is said to have the advantage that slow-moving displacements, such as those due to breathing, are not recorded, and the deflections in the record are actually proportional to the kinetic energy imparted to the body by the discharge of blood.

Henderson believes that the volume of the systolic discharge per unit body area may be obtained by dividing the distance that the body has moved by the height of the individual.

Heald and Tucker demonstrated that the amplitude of the recoil curve increases under such conditions as give rise to increased systolic discharge. Thus, they found that the amplitude of the curves increased after nitroglycerine and exercise, and was larger also in a case of aortic regurgitation. That the amplitude is not necessarily governed by the volume of systolic discharge alone is indicated by the fact that the curves are much larger during inspiration than during expiration. Consequently, as these investigators also point out, the part that is played by position changes in the heart, by changes in distensibility in the aorta, etc., must be more extensively studied before its clinical applicability will have been demonstrated.

CLINICAL ASPECTS OF BLOOD-FLOW DETERMINATIONS.

Normal Values.—The values obtained by individual observers using not only different methods, but different technical refinements in the same methods, may profitably be tabulated, not so much because equal significance attaches to all, as far as normal ranges of blood volumes ejected by the ventricles are concerned, but rather because it is necessary in evaluating reports on blood flow determination under abnormal conditions to make continued reference to such "normals" as were established by comparable methods.

Author.	Number of subjects.	Minute volume, cc.	Systolic discharge, cc.
Loewy and Schrötter	12	4089–10700	33–139
Plesch	5	2732–5334	40–78
Schapals	2	4531–4995	43–84
Zuntz	1	2844–6676	48–97
Müller	4	4500–5500	55–65
Krogh and Lindhard	3	2800–8700	39–103
		4000–4100 R	
Lindhard	15	4900–9400	78–151
		4000–7200 R	51–117 R
Boothby	1	3500	60
		3400 R	58 R
Lundsgaard	2	4800–10000	51–75
		3800–6000	
Lindhard and Hasselbalch	2	4000–7500(R?)	
Fridericia	2	4100–6500	61–98
Liljestrand and Lindhard	..	3300–3600	44–50
Douglas and Haldane	..	3900–4300	54–60
		5000–8000	70–120
Barcroft and Roughton	..	6800	?
Henderson	1(?)	9240	132
Meek and Eyster	17	1474–15636	17.7–232
Average	..	5914	79.4

R = calculations based on figures "reduced" to apparently "normal" conditions.

While it is undoubtedly too early to reach final conclusions as to normal values of blood flow in man, a survey of the table indicates that they show fairly concordant values. Roughly speaking, we may say that the systolic discharge in man during rest probably varies from 50 to 80 cc, and that the minute volume ranges from 3500 to 5600 per minute. Calculations on a basis of blood flow per 100 gm. show average values ranging from 6 to 8.5 cc per minute. This accords reasonably well with blood-flow determinations in the extremities, for Hewlett and his co-workers found a variation between 2 and 8 cc per 100 gm. arm substances per minute, while Stewart obtained figures ranging from 3.5 to 14 cc of blood flow per 100 gm. per minute. In comparing the results obtained through improved methods of Douglas and Haldane with those obtained by the nitrous-oxide method (especially those of Krogh and Lindhard, Boothby, Fridericia, Liljestrand and Lindhard), it is at once obvious that Douglas and Haldane obtained a much greater minute volume and systolic discharge for normal men at rest. These investigators would place the normal minute volume at 5 to 8 liters and the systolic discharge between 70 and 120 cc. They are inclined to attribute these differences to the inadequacy of the nitrous-oxide method. Calculations made by Barcroft and Roughton on a single individual, both on the basis of the procedure suggested by Henderson as well as their own, tended to suggest that the minute volume is in excess of 6 liters per minute. Henderson's recent results obtained by a simplified method indicate that the minute volume discharged is

normally over 9 liters. The results of Meek and Eyster obtained by an entirely different method agree closely with former averages.

During muscular exercise, the systolic discharge and minute volume are generally considered to increase greatly. Thus, Krogh and Lindhard found the tremendous increase in minute volume from normal to 17,200 and 21,200 cc in two different individuals. At the same time the systolic discharge increased greatly (113 cc). While this was also the case in most of the experiments reported by Douglas and Haldane, they nevertheless stress the fact that the increase in minute volume may occur, *pari passu*, with the increase in pulse rate. In such cases, the increased minute volume is obviously not accompanied by increased systolic discharge. Similar results are reported by Henderson, but no data are given. Meek and Eyster, on the contrary, find that both systolic discharge and minute volume increase greatly during exercise. At high altitudes the minute volume either remains unchanged or increases slightly (Hasselbalch and Lindhard). Passive movements and massage cause no increase in minute volume (Liljestrand and Stenström).

Pathological Cases.—In many pathological conditions of the circulation, the volume flow is practically unchanged, indicating that the circulation is efficiently carried on in spite of pathological processes. This is frequently the case where there is distinct evidence of valvular lesions (Newburgh and Means). Plesch found the average flow per 100 gm. actually increased in some instances. When decompensation occurs, however, the volume flow decreases, especially in the limbs (Stewart, Hewlett and Van Zwaluwenburg). Lundsgaard, on the other hand, reports diminished minute volumes also in cases of compensated valvular lesions (mitral stenosis).

The reduction in the peripheral volume flow is greatest in cases of heart irregularities and where there are other evidences of myocardial impairment. Thus, Lundsgaard has recently reported a case of total heart-block with a pulse rate of 40, which, nevertheless, had a normal minute volume during rest. During exercise the usual increase could not, however, be attained. Barcroft, Bock and Roughton also report a case in which the minute volume decreased during an attack of paroxysmal tachycardia from a normal minute volume of 5 or 6.1 liters to 2.8 or 2.1 liters per minute. In this case the estimated systolic discharge decreased from 77.5 to 12.9 cc. In auricular fibrillation the minute volume is reduced (Lundsgaard).

The peripheral flow is markedly reduced in arteriosclerosis and no further reduction of flow is obtained by dipping the opposite hand in cold water (Stewart).

The minute-volume, as also the peripheral volume-flow, is distinctly increased in cases of exophthalmic goiter. Plesch found an average minute volume of 5286 cc with a flow per 100 gm. of 9.73 cc per minute. Stewart also found an exceptionally large flow in the hands (14.18 cc per 100 gm. per minute).

In anemias a curious relation between the minute volume and peripheral flow seems to exist. Plesch found a large increase of minute volume, averaging 9083 cc, giving a flow of 13.23 cc per 100 gm. per second. The increase is greater than is accounted for by the heart rate, since the pulse volume equaled 142.9 cc. The peripheral volume flow, however, is diminished by anemias, less in chlorosis than in other forms. Stewart regards this as a compensatory endeavor on the part of the peripheral mechanism to divert the blood from the periphery to the more vital organs, in this way assisting the return of blood to the heart and lungs by shortening the circulation time.

VENOUS PRESSURE MEASUREMENTS.

Methods and Technic.—Method of Gaertner.—This method, which was primarily suggested but not developed by v. Frey, is based upon the principle that the veins of the extremities represent a manometer column in communication with the auricle; hence, if the arm is raised they collapse when the hydrostatic pressure within them counterbalances the pressure in the right auricle. The following procedure is usually followed: With the subject seated erect before the measuring apparatus, the position of the center of the costosternal angle is first ascertained. The experimenter then supports the *relaxed arm* of the subject by the elbow and the hand, bending the arm at an angle of 120 degrees. With a good illumination on the back of the hand, the whole arm is raised to such a level that the veins collapse. The distance between this level and the point fixed on the chest is then measured by the aid of a meter rule or by a special set of pointers. It represents the auricular pressure in centimeters of blood, which approximates water in its specific gravity sufficiently closely so that it may be translated without correction.

v. Recklinghausen has suggested the following convenient though rougher modification for bedside use. The one hand of the patient in recumbent posture is allowed to rest by his side on the bed, the other is placed on the thigh. If the veins of the latter collapse while those of the former fill, normal pressure relations exist. If the veins of both collapse venous pressure is low. If the veins of both fill, venous pressure is high.

Method of v. Recklinghausen and its Modification (Fig. 130).—The principle first suggested by v. Recklinghausen consists in exerting a pressure over some superficial vein by a transparent device through which the collapse of the vein can be observed. The essential parts of the apparatus consist of a water manometer for measuring the pressure, a bulb for increasing or decreasing it, and, in addition, a device for applying it to the vein. This pressure box has been given several forms. In v. Recklinghausen's apparatus it consists of a small rubber bag (5.5 cm. in diameter) with an opening in the center.

Over the top of this a glass plate is laid. Eyster and Hooker substituted for this a small glass pressure box covered below with rubber in which an opening had been cut. The writer has used for some years an ordinary thistle tube, the stem of which was cut off and bent and the flange of which was covered with rubber dam with an opening in the center. Recently, Hooker has similarly employed a light glass cup, 20 mm. in diameter, which may be used without the rubber dam (Fig. 130, *A* and *B*).

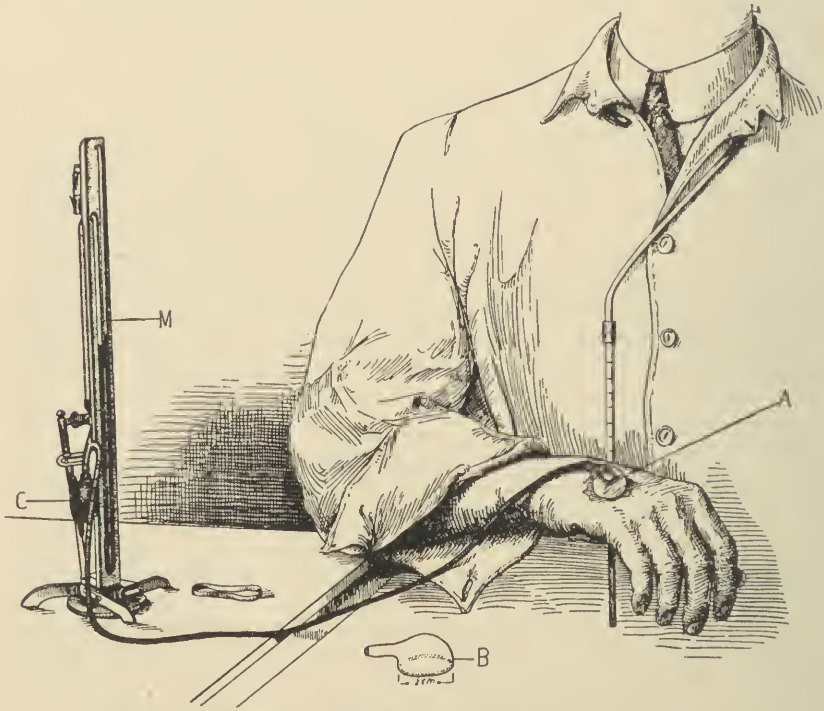

FIG. 130.—Hooker's venous pressure apparatus. (From Norris.)

The ring of the v. Recklinghausen apparatus is fitted air-tight to the skin coated with glycerine and the top is covered with a glass plate. The older pressure box of Eyster and Hooker and the thistle tubes as well are similarly rendered air-tight, but are held on by tapes or straps. In the recent modification of Hooker, the chamber is only temporarily held with a rubber band encircling the hand. It is then cemented to the skin by a film of collodion allowed to fill in the angle formed between the skin and the glass cup.

The technic consists in applying this chamber to the vein of a passively resting arm and raising the pressure within the system until the vein under good illumination collapses. Some degree of

judgment is required to decide this point exactly. According to Hooker, the most consistent results are obtained when the reading is made at the point where slight oscillations of pressure cause the vein shadows to come and go quickly. The pressure reading thus obtained must be corrected by adding or subtracting the hydrostatic column between the level of the vein and the mid-point of the sternal angle, which is arbitrarily taken as the right auricular level, as in Gaertner's method. This is conveniently done by suspending a scale by a loop around the subject's collar, as shown in Fig. 130.

Venous Pressure Gauges.—If the blood is stroked out of a superficial vein in the direction of the heart, the vein collapses as far peripherally as the next venous valve. Both Oliver and Sewall have devised instruments, called *pressure gauges*, which replace the finger and exert a variable pressure on the vein. By totally compressing it and then releasing the button until the blood just flows through, the pressure exerted by the peripheral venous blood may be estimated by a spring gauge. To obtain accurate comparisons, the readings are corrected for the hydrostatic differences between the level of the vein and the costosternal angle, as in the methods of Gaertner and v. Recklinghausen.

Plethysmographic Method.—Two cuffs are applied, one to the upper arm and the other to the forearm. The forearm cuff serves as a plethysmograph and, hence, is very slightly inflated so as to exert a very little pressure (not more than 1 cm. water). It may be connected to a water manometer or some form of recording tambour (Frank and Reh). The upper cuff is then very slowly inflated until the volume and pressure in the lower cuff increase, due to the damming back of blood when the veins of the upper arm are compressed.

Direct Measurement.—The direct measurement of venous pressure is carried out, after the description of Moritz and Tabora, by aseptically inserting a needle into the median vein of the forearm and allowing a sterile saline solution to slowly enter from a burette graduated by a millimeter rather than a centimeter scale. When the inflow ceases, the level of the saline above the level of the heart represents the venous pressure in millimeters of water (Fig. 131).

Clinical Value of Accurate Venous Pressure Determination.—The procedures for determining the venous pressure so far described have been largely used to study its height and variation in normal cases. Thus, it has been determined by Hooker and Eyster that the corrected auricular pressure varies from 2 to 16 cm. of water, although Hooker obtained somewhat higher figures with his newer apparatus. During exercise the pressure rises to 17 to 22 cm. of water. The venous pressure undergoes diurnal variations, rising from 10 to 20 cm. during the day and decreasing by a corresponding amount during the night, the average pressure during the day being about 15 cm.

The venous pressure is regulated by the intrathoracic pressure. When this approaches atmospheric, the venous pressure rises, and *vice versa.*

Local dilatations and contractions, such as are induced by heat and cold, may not affect the venous pressure, thus showing that a relation does not necessarily exist between the venous pressure and the caliber of the vein. This leads to the conclusion that the prominence of the veins is not always an index of the venous pressure.

FIG. 131.—Moritz-Tabora's method of estimating venous pressure. (After Hoffman.)

Clinically, the value of accurate venous pressure measurements has not been sufficiently developed to warrant a statement concerning their possible diagnostic significance.[1] Eyster and Hooker report a few cases showing a higher pressure in pathological conditions, and Sewall believes that more information may be gained by com-

[1] For a recent analysis of factors affecting venous pressures and thus rendering their clinical value doubtful, *cf.* Kroetz (Deutsch. Arch. f. klin. Med., 1922, **139**, 325).

paring the ratio of venous and arterial pressures. He divides the clinical cases with disturbed venous pressures into the following classes:

(*a*) Those in which the ratio of arterial to venous pressure is increased. This is due to a positive elevation of arterial pressure in such disorders as vasomotor spasm, increased viscosity of the blood and arteriosclerosis.

(*b*) Those in which the ratio of arterial to venous pressure is decreased. This is due to a positive elevation of the venous pressure caused either by physical obstruction of the output of the right heart or by functional changes of intermediary metabolism.

(*c*) Those in which the ratio of arterial to venous pressure is not materially changed but both are abnormally high. In these conditions a general plethora exists.

(*d*) Those in which the ratio of arterial to venous pressure is not materially changed but both are low. In these, a condition of asthenia or decompensation is imminent.

The following table, compiled by Austin in Norris's volume on blood-pressure, summarizes the variations in venous pressures obtained by different observers:

Venous pressure.	At heart level cm. of H_2O.	Normal mm. Hg.	Pathological. cm. H_2O.	mm. Hg.
Sewall	4.6– 5.2	3.4–3.8		
von Basch	8.8	6.5		
von Recklinghausen (filled)	14.0–22.0			
(veins empty)	20.0–26.0			
Hooker-Eyster	3.0–10.0	2.2–7.3		
Frank and Reh	1.0– 6.0	7.0–4.4	to 17	to 12.5
Howell	4.0–13.0	2.9–9.5	7–25	5.1–18.4
Moritz and Tabora	1.1– 8.7	0.8–6.4		
Briscoe	87.–10.5	——	10.6–11.5	
Summary	1.0–13.0	0.7–9.5	up to 25	up to 18+

The Effective Venous Pressure.—The significance and clinical value of exact venous pressure measurements is, no doubt, minimized by the fact that the filling of the heart is not determined, as in the opened chest, by the actual venous pressure but by the "effective venous pressure," as the difference between intrathoracic and venous pressure is called (*cf.* page 105). It follows that any increase in intrathoracic pressure may increase the extrathoracic venous pressure without any disturbance of cardiac activity. Unless it can be assumed that intrathoracic pressure remains unchanged, or unless some simple and safe method for its simultaneous determination can be found, the value of venous pressure measurements in pathological cases is not evident.

CAPILLARY BLOOD-PRESSURE MEASUREMENTS.

Apparatus, Technic, Critique.—Methods Based upon Blanching of the Skin.—Practically all of the earlier models of capillary tonometers

were based upon the principle first used by v. Kries, viz., that paling of the skin is determined by compression of the capillaries. Consequently, the amount of pressure necessary to produce such blanching was considered a measure of capillary pressure. The principle has been employed by v. Basch, v. Recklinghausen and Basler.

In practice it is, however, difficult to obtain concordant consecutive readings whether one observes, as did v. Kries, the pressure which first produces a visible pallor, or as did v. Basch, the pressure which causes complete blanching, or as did v. Recklinghausen, the pressure at the instant the skin first begins to blush (Lombard). Furthermore, anatomical as well as experimental considerations render it probable that blanching of the skin is determined rather by the emptying of the smaller venous plexuses of the skin (Lombard, Danzer and Hooker).

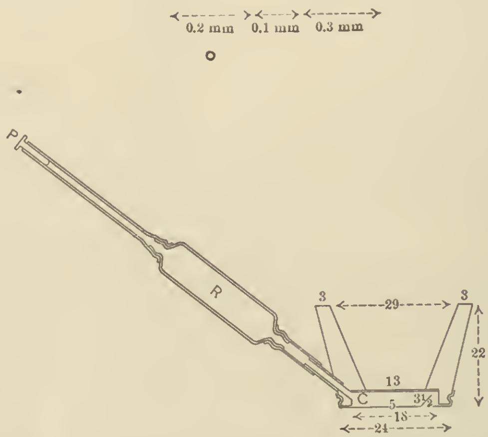

FIG. 132.—Diagram showing pressure chamber of Lombard tonometer for measuring capillary pressures in the skin. Description in text. (After Lombard.)

Methods Based upon Direct Observations of the Capillaries.—This method owes its existence to the discovery by Lombard that, when a drop of glycerine or oil is placed upon the skin and the area is illuminated by an intense light, the cuticle becomes transparent and permits an examination of the capillary tufts by means of a low-powered microscope.

In order to estimate the pressure, Lombard constructed a small pressure chamber, shown diagrammatically in Fig. 132. This consists of a brass cone with a pressure chamber, *C*, at the bottom. The roof, 13, is covered by a cover-glass and the bottom, 5, with goldbeaters' skin, in the center of which a round opening is cut. The pressure is increased by forcing additional but small amounts of glycerine into the chamber, *C*, through the attached tube, *R*. The external pressure at which capillary flow ceased is taken as capillary pressure.

Lombard emphasizes that this pressure varies considerably in different capillaries, a fact which makes it difficult to give a single figure for capillary pressures.

The principle has also been employed in the microtonometers devised by Kraus, Basler, Kylin and Danzer and Hooker. The microcapillary tonometer of the last-named investigators is shown in Fig. 133. Aside from details in construction, it differs from the Lombard pattern in that the bottom of the pressure chamber, 7, is entirely closed by goldbeaters' skin, which is rendered transparent by being previously treated with glycerin and castor oil. Danzer and Hooker selected the skin area at the base of the nail as best suited

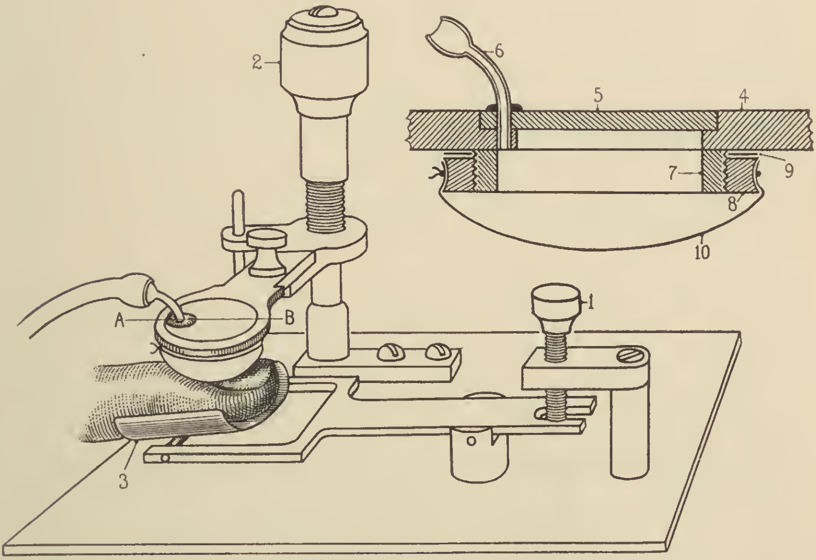

Fig. 133.—Danzer and Hooker's capillary tonometer. Description in text. (Courtesy of Danzer and Hooker.)

for observation, because here most of the capillaries pursue a horizontal course and a number of vessels may, therefore, be brought into focus at the same time. Inasmuch as the capillaries are often not emptied of their blood during compression, and as the blood flow often reverses when an excessive pressure is applied, Danzer and Hooker suggested as a criterion of capillary pressure the point where, on the reduction of pressure, the stream again begins to move forward. As this point is reached at slightly different pressures in different capillaries, Danzer and Hooker take the mean of several capillaries observed as an index of capillary pressure. They suggest that a series of six or more capillaries be taken into consideration in which the difference in pressure is not more than 6 or 7 mm. As

regards the criteria for estimating capillary pressure, L. Hill points out that the pressure which stops the flow does not indicate capillary pressure, but rather the pressure in the supplying arterioles. He, therefore, suggests the point where the capillary flow begins to lessen as a more correct criterion of capillary pressure.

Normal Values for Capillary Pressures.—As already intimated, observers are agreed that the pressure in different capillaries examined in any given area varies. Thus, Lombard divides the capillaries into three classes: The smallest capillaries yielding to pressures of 15 to 20 mm., the medium capillaries compressed at pressures of 35 to 45 mm. and the larger capillaries requiring a pressure of 60 to 70 mm. Hg. The average pressures in the most compressible capillary they placed at 15 to 25 mm., however. Danzer and Hooker report examinations on 6 children and 25 adults between the ages of eight to forty-seven years. The lowest average capillary pressure found was 17.5 mm. Hg., the highest 26.5 mm. Hg. They regard 22 mm. Hg. as a mean normal pressure. Other observers, however, report somewhat lower values. Thus, Kylin places the average capillary pressure at 10 mm. Hg., Basler at 12 cm. water, Hill at 10 to 12 cm. of water. These variations are due, as before explained, to the different criteria for capillary pressure employed by investigators.

As to the variation of capillary pressure, experimental work indicates that cold lowers and heat raises capillary pressure. The pressure in the capillaries is lowest in the recumbent and highest in the standing position. The pressure is raised whenever the intrathoracic pressure increases and by venous compression from any cause.

Pathological Variations.—The measurement of capillary pressures in clinical disorders of the circulation opens a fruitful field for investigation, but as yet reports by the more reliable methods are somewhat scanty. Kylin observed abnormally high capillary pressure in cases of glomerular nephritis and scarlet fever. The highest pressures recorded in such cases were 40 to 50 mm. Hg. (as compared to his normals of 10 mm. Hg.). These observations are apparently confirmed by Thaller and Draga as well as by Weiss, but disputed by Schur and Boas-Frant, who employed the apparatus and technic of Danzer and Hooker. The latter investigator was able to divide cases with hypertension into two groups, viz.: (*a*) Those in which the capillary pressures may range between 21 and 70 mm., but usually between 30 and 60 mm. Hg.; and (*b*) those having normal capillary pressures, *i. e.*, below 30 mm. Hg. They conclude that cases of hypertension with a high capillary pressure suffer from a general capillary disease, of which a coincident glomerular nephritis is only one manifestation. In so-called essential hypertension, the capillary pressure is low. Briscoe reports high capillary pressures

(30 to 50 cm. water) in blue-handed patients, classified as "irritable heart." It is interesting to note that venous pressures were relatively little affected.

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CHAPTER XIX.

THE ROENTGENOGRAM AND ORTHODIAGRAM.

PHYSICS, APPARATUS AND TECHNIC IN ROENTGEN-RAY EXAMINATION OF THE HEART AND LARGE VESSELS.

WHENEVER electrons, traveling at high rates of speed, are suddenly checked by a target of high atomic weight, certain vibrations, known after their discoverer as roentgen or x-rays, are produced.

These rays differ from ordinary light rays in that they are themselves invisible, penetrate obstacles in accordance with their atomic weight and not according to their molecular arrangement, are not refracted by prisms, concentrated by lenses nor reflected from the highest polished surfaces so far made. They resemble light in that they are a form of transverse vibration of the ether (though of much higher frequency) and also produce chemical effects upon photographic plates and animal tissues. Their value in studying the intrathoracic organs lies in the fact that the penetrating power of the rays depends upon the density of the structures through which they have to pass. The heart and large vessels, for example, on account of their high atomic weight, absorb a larger number of rays than the air-containing lungs which, by contrast, allow the rays to pass better. By placing on one side of the chest a roentgen-ray tube and on the other a photographic plate or a fluoroscopic screen which is rendered luminous by the penetrating rays, the shadows of the heart and large vessels can be clearly distinguished from the lungs.

Physical Principles in Roentgen-ray Production.—The generation of roentgen-ray in tubes involves four distinct processes: (1) The separation of negatively charged electrons (also spoken of as cathode rays) from atoms; (2) imparting to them a high velocity; (3) concentrating or focussing them upon a relatively small area; (4) suddenly checking their velocity.

The separation of negatively charged particles or electrons may be accomplished either by a "gas tube" or a thermionic tube (Coolidge tube). The former consists of a tube in which a partial vacuum is created and the liberation of electrons depends upon the breakdown of gas atoms within the tube by the combined effects of: (*a*) A high potential discharge through the tube from the anode to the cathode (*cf.* Fig. 134); (*b*) the movement of electrons; (*c*) by the generated roentgen rays themselves. This type of tube has the disadvantage that the supply of electrons is somewhat uncertain and

not controllable. In the so-called electron tube first made practical by Coolidge, all the gas capable of breaking down is removed by

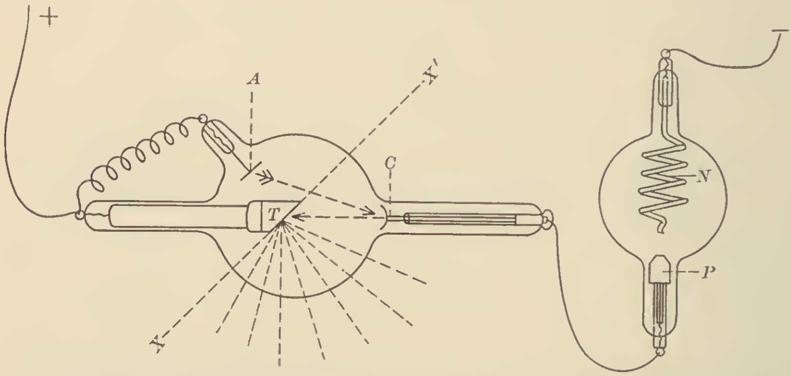

FIG. 134.—Diagram showing roentgen-ray tube and ventral tube in series: *A*, anode; *T*, target; *C*, cathode; *P*, aluminum electrode, and *N*, spiral electrode.

the creation of a high vacuum and the electrons are derived from the atoms of a heated tungsten wire (Fig. 135, F). As the temperature

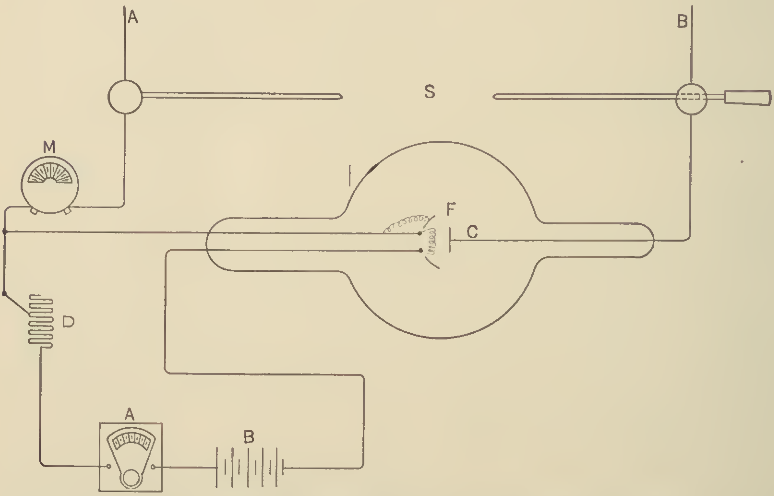

FIG. 135.—Diagram showing component parts of the Coolidge roentgen-ray tube and electrical circuit for heating the Tungsten filament, *F;* also current connections for discharging high voltages through tube. *B*, storage battery; *A*, ammeter; *R*, resistance controlling the heating of the spiral filament, *F; A* and *B* (above), connections for high-tension current; *S*, spark-gap. (After Knox.)

of this filament can be controlled by varying the heating current and the number of electrons given off is determined by the tempera-

ture, it is under definite control. Recently, Lilienfeld reports that he has been able to release electrons from an unheated or cold cathode in the absence of any kind of ionization. He believes that this liberation of electrons is due primarily to the electrostatic field itself, and, consequently, has designated the process as "auto-electronic."

In order to impart a high velocity to the electrons, a high voltage must be discharged through the tube. Most roentgen-ray tubes require only a low current (5 to 100 m/a.), but the voltage must range between 25,000 to 100,000. This requirement has been met in several ways: The static machine, at first almost entirely used, supplies such a current, but has proven unsatisfactory in roentgenographic examination of the thoracic organs, since the current is not of sufficient intensity to permit as short an exposure as desired and the apparatus is subject to periods of unsatisfactory performance. The induction coil which generates a current of greater intensity and high voltage was next brought into service. As is well known, this consists of a primary coil and some special form of automatic interrupter supplied by a constant current from an electric light circuit or storage battery. The current produced in the secondary coil by induction has the disadvantage of being alternating in character, and the reason that it can be used with roentgen-ray tubes at all lies in the fact that, owing to self-induction in the primary on the "make," the current in one direction is far stronger than in the other, thus giving a current predominating in one direction. This *inverse current,* as the make current is called, is deleterious, however, both because it gives rise to stray roentgen rays and also because it shortens the time a tube remains usable. Various devices for preventing the entrance of the inverse current into the tube or for converting it into a current of opposite direction have been devised. The simplest procedure is to place the tube in series with a spark gap, across which the inverse current cannot leap. Its passage is more satisfactorily prevented, however, by placing a *ventil tube* or *valve tube* in series. This device (Fig. 134) consists of a vacuum tube with two electrodes, one of which, *P*, is a small aluminum affair, the other, *N*, a long spiral of greater surface. When the direction of the current is such that the spiral, *N*, is the cathode, the current passes readily, whereas its passage is entirely prevented when it becomes the anode. As the valve tubes have, however, the disadvantage that they waste considerable electrical energy, the negative variation of the alternating current is now more generally converted into positive variations by the employment of current inverters, or rectifiers. Such a device may be constructed by fastening two copper commutator strips attached to a rotating mica disk of a synchronous motor in such a way that they are opposite each other and occupy a little more than a quadrant of the circle. When the disks revolve contacts are made so that first one of the alternating high-tension brushes and then the other

connects through the strips with the brushes leading off the current. In this way a regular series of unidirectional potential variations are led off without appreciable loss of energy. Such valve tubes or rectifiers are even more needed when the current supplying a roentgen-ray tube is generated by a step-up transformer; for an alternating high-voltage current so generated, unlike that from the induction coil, is equal in each direction and is itself entirely useless unless the current is unidirectional. Although a unidirectional current is always more economical, the new Coolidge tube with a radiator-cooled target can be used with an alternating current, as it in itself acts as a valve tube as long as the focal spot is kept at a temperature sufficiently low that it does not give off electrons. In the gas-filled tube, the positive terminal of the high-tension current so generated is connected to both the anode and target or anticathode (Fig. 134). In the Coolidge tube, the target also serves as an anode. In this connection it may be pointed out that, inasmuch as these tubes contain no conducting gases, currents can be discharged through the tube only when electrons are being liberated by heating the tungsten spiral filament. Furthermore, the current that can be discharged through the tube is limited for any particular temperature. When the temperature of the filament is low, only a small number of electrons are produced and, consequently, only a relatively small current can be carried through the tube no matter how high the supplying voltage.

When a suitable high-tension current is thus applied, the negatively charged electrons are driven at great velocity from the cathode to the target. The site of the area or the so-called "focus" upon which the electrons are directed depends upon the construction of the cathode. Consequently, tubes are said to have a fine or broad focus. The finer the focus, the clearer the definition when small objects are examined; but the broader it becomes, the more readily heat is removed by conduction and the smaller the degree of burning or pitting of the target. The cathode differs in shape and size in the different patterns of gas tubes, but is always made of aluminum. In the Coolidge tube, the cathode stream is focussed by a spiral cylinder of molybdenum which surrounds and slightly projects over the heated tungsten coil (Fig. 135).

The cathode serves to check suddenly the bombarding cathode rays or electrons. In order to convert as large a part of the energy into roentgen rays as possible, the target must be made of metal with high atomic weight. As a large proportion of the energy at best is converted into heat, the material of the target must also have a high melting-point, no vaporization and must conduct heat readily. Formerly, platinum was extensively used, but of late years tungsten has been preferred.

The definition shown in a roentgenogram, as the photographic plate or print is termed, depends upon the character of the tube

used and its adaptation for the object to be transillumined. Roentgen-ray tubes are classified as "hard" and "soft" in accordance as their vacuum is high or low and the penetrating power of the rays generated, great or small. It is possible to obtain tubes of such hardness that even the bones are readily penetrated. In obtaining roentgenograms of the intrathoracic organs, medium-hard tubes seem to be preferable, for in roentgenograms so obtained the shadows of the sternum and vertebræ are less prominent and the heart shadow is consequently clearer.

The tendency of all gas tubes is to harden with use, and many devices have been introduced by means of which the tubes can again be softened. They embody one or the other of the following principles:

1. Discharging a small current through a side tube containing some non-inflammable material, and thereby liberating gas.
2. Allowing a small amount of air to enter through a mercury valve.
3. Bombarding a special volatile target by rays from an auxiliary cathode.
4. Allowing small quantities of hydrogen to enter through a fine palladium tube.
5. Heating the entire tube was formerly practised.

Technic of Roentgen-ray Examination.—The transillumination of the chest is usually made in a dorsoventral (tube behind, plate in front) or a ventrodorsal (tube in front, plate behind) direction, because the best definition can be so obtained. Exposures in lateral or diagonal planes are sometimes necessary, however, for supplementary information. In taking *roentgenograms* of the heart, it is desirable to make the exposure so brief that it can be obtained at the height of a natural inspiration. By proper selection of the tubes and plate and by covering the plate with an intensifying screen, it has been found possible to obtain roentgenograms in a fraction of a second. These intensifying screens are plates coated with some substance, such as calcium tungstate, which allows all the roentgen rays to pass readily and, in addition, becomes luminous and so more readily affects the plate.

Formerly, the roentgen-ray tube was placed about 60 cm. from the back of the chest and the plate within its light protecting envelope in contact with the anterior chest wall.

Since the roentgen rays emanating from the target are divergent, it becomes evident that the heart shadow must be larger than the actual size of the heart (Fig. 136); furthermore, that the degree of enlargement depends upon: (*a*) The proximity of the plate and tube to the chest, and (*b*) upon the proximity of the heart to the tube. Thus, the base of the heart which lies posterior to the apex is enlarged more than the apex. It follows that only by keeping the plates and tubes at exact distances from the chest in different sub-

jects or in subsequent observations upon the same subject can even an approximately correct idea of the heart area be obtained. Even so, the roentgenogram should be regarded as qualitative and not quantitative. Various attempts have been made to overcome this artificial enlargement of the heart area. All efforts to convert the divergent rays into parallel rays have failed. If, however, the tube is removed to a greater distance from the chest, the rays become more nearly parallel and the error is greatly diminished. Only recently has it been possible to use tubes at a distance of 2 meters and obtain roentgenograms within an exposure time of one and a half to two seconds. Plates so obtained are termed *teleroentgenograms.* According to Bardeen, this gives a heart silhouette only 6 per cent larger than the shadow projection should be.

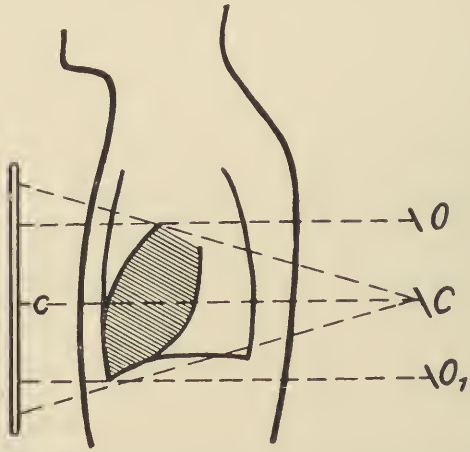

Fig. 136.—Diagram illustrating the difference in the size of the shadow when protected by divergent and parallel rays. (After Groedel.)

The method of teleroentgenography is carried out as follows: The patient is given a glass of water which may be made effervescent in order to aid in outlining the apex in the shadow. The patient stands or sits so that the sternum is flat against a vertical light-protected plate. The suprasternal notch and angle of Ludwig or the spine of the ninth thoracic vertebræ may be marked by a lead marker. The target of the roentgen-ray tube is placed at a distance of 2 meters (about 6½ ft.) at a level with the ninth thoracic vertebræ. The patient may hold his breath in moderate inspiration, but it is preferable to make a rapid exposure during natural inspiration, using an intensifying screen for the purpose.

In 1900, Moritz devised an apparatus, the *orthodiagraph,* which, as improved upon by subsequent workers, offers the most exact method of determining the heart area. The principle of the ortho-

diagraph may be explained by reference to Fig. 136). If the target of a roentgen-ray tube be shifted so that the central rays, *c c*, emanating from it at right angles to the body axis touch the heart boundaries tangentially, as at O and O_1, the heart shadow will be projected by parallel rays upon the screen. It should be borne in mind, however, that, on account of the sloping position of the heart, neither the dorsoventral nor the ventrodorsal orthodiagram, as the record is termed, gives it correct anatomical length. Fortunately, however, the correct breadth is more nearly projected.

The technic of operating an orthodiagraph can be only briefly described in this book. For a more comprehensive description, the small volume by Groedel may be recommended. Fig. 137 illustrates one form of this apparatus, which may be used either in horizontal

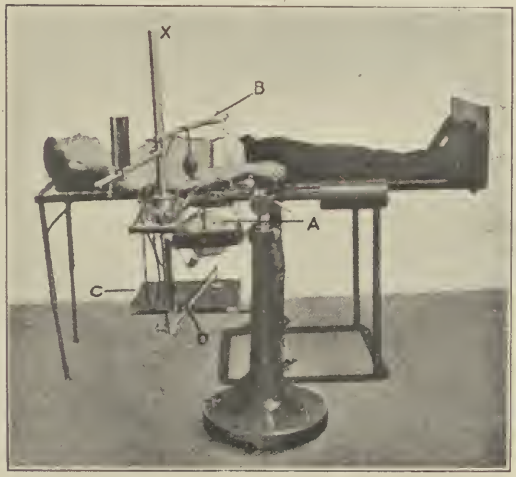

Fig. 137

or vertical posture. The patient lies upon a table beneath which the roentgen-ray tube, A, is held. Fastened to the same vertical arm, X, is a small screen, B. Upon this screen is a mark centered so that it is directly over the middle of the anticathode. By a special mechanical device these two points move together in various directions so that the same central rays pass between them. Any point of the heart border during diastole, which is visible upon the screen is made to coincide with the mark upon the screen. By tracing this mark around the heart and lung borders they may be outlined and graphically recorded upon a parallel plane, C, below the table by a pencil, D, which is in line with the target and mark. The record so obtained is called an *orthodiagram*. Since an interval of time must naturally elapse before the heart can be outlined, it is necessary to allow the patient to breathe quietly. These respiratory movements

and the movements of the heart itself are factors which interfere slightly with a correct projection of the heart, and, together with the personal equation of the operator, constitute the greatest source of the error incurred in orthodiagraphic work. Various procedures, as stereoscopic pictures and kinematographic pictures of the heart, as well as instantaneous roentgenograms at various phases of the heart cycle (Bardeen, Eyster and Meek) are being tested with the hope of obtaining still better methods of outlining the heart and studying its action within the closed chest.

FIG. 138.—Normal radiogram of heart during inspiration. (After Groedel.)

THE NATURE AND SIGNIFICANCE OF NORMAL TELEROENTGENOGRAMS AND ORTHODIAGRAMS.

In Fig. 138 is shown a roentgenogram taken in the dorsoventral diameter (tube behind). Aside from the shadows of the bony structures, which do not concern us, the positive print shows two lateral light areas, in each of which a fringed shadow indicates the roots of the lungs. Central to this appears the flask-shaped darker shadow of the heart and large vessels. The shadow is not equally dense throughout, but owing to the air-containing trachea is distinctly lighter in its upper portion. Upon fluoroscopic examination it is observed that the right portion (Fig. 138, *A*) undergoes a very slight presystolic contraction. The lower left border, *C*, shows a systolic

increase in size while the upper border, *D*, slightly later shows a systolic enlargement. In the orthodiagram (Fig. 139) we recognize two distinct arcs on the right and three on the left boundary of the heart. By the nature of the pulsations just described, as well as by postmortem examination, it has been established that the upper right arc bounds the aorta (occasionally the vena cava) while the lower encircles the right auricle. On the left side, the upper arc marks the boundary of the aorta, the second that of the pulmonary artery, while the lower arc indicates the left ventricle. The shadow of the right ventricle merges with that of the diaphragm below.

Standards of Comparison.—It is obvious that the size of the heart, as reflected in teleroentgenograms and orthodiagrams, must vary with body weight, height and size and possibly also with other conditions. It is necessary, therefore, to have certain standards with

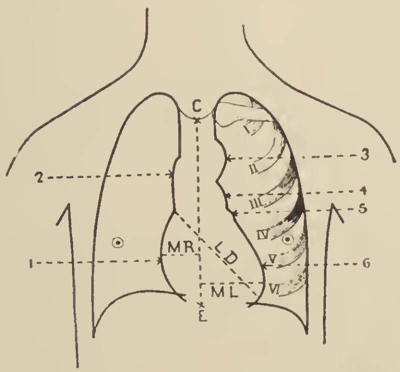

FIG. 139.—Orthodiagram of normal heart. 1, right auricular curve; 2, great vessels curve; 3, aortic curve; 4, pulmonary curve; 5-6, left ventricular curve. *M R*, median right diameter; *M L*, median left diameter; *T D*, sum of *M R* and *M L; L D*, longitudinal diameter; *C E*, central line.

which pathological cases may be compared. This has been done in various ways. The area of the heart silhouette may be determined by means of a planimeter. Owing to the facts that the apex of the beat is not always clearly defined and an arbitrary line must be taken as demarcating the ventricles and large vessels, this method has not been generally employed. According to the system introduced by Moritz, it is customary to measure (Fig. 139) the greatest distance to the right and left of the median line, *M R* and *M L*, the total transverse diameter, T ($= M\ R + M\ L$), and the diagonal length, *L D*. Of these measurements, the greatest transverse diameter is probably the most exact and, therefore, the one most frequently made. Bardeen, in restudying the subject, has pointed out that the total surface area, as determined by a planimeter, bears a definite relation to the body weight and height and, as anatomical studies

on cadavers led him to believe, also gives an approximate index of the heart weight and heart volume in diastole. The following formulæ are proposed:

Body weight in kilos = 1/20 H $^3/_2$, where H is area of heart silhouette in cm.
Heart weight in grams = 1/20 H $^3/_2$ × 0.0055
Heart volume in grams = 0.53 × H $^3/_2$

Adopting these different standards, various authors have compiled tables and charts as to normal values.

The following table, compiled from the combined results of Dietlen, Groedel and Verth, gives average sizes and diameters at different ages and in individuals of different body weight and size.

Position.	Size, cm.	Sex.	Age.	MR.	ML.	L.	Author.
Horizontal . .	145–154	Male	20 or over	3.70	8.50	13.4	Groedel.
" . .	155–164	"	" "	4.20	8.70	14.0	"
" . .	165–174	"	" "	4.30	8.80	14.2	"
" . .	175–187	"	" "	4.50	9.30	14.9	"
" . .	145–154	"	15–19	3.50	7.50	11.8	"
" . .	175–182	"	15–19	4.00	7.90	13.7	"
Vertical . .	145–154	"	Grown	4.70	8.00	12.9	"
" . .	175–185	"	"	4.70	8.50	14.2	"
" . .	145–154	"	Before puberty	3.90	7.40	11.8	"
" . .	175–187	"	" "	4.00	8.00	13.7	"
Horizontal . .	145–154	Female	17 or over	3.50	8.30	12.8	Dietlen.
" . .	165–174	"	" "	3.70	8.80	13.6	"
" . .	145–154	"	15–17	3.50	7.50	12.4	"
" . .	165–174	"	15–17	3.40	7.70	12.7	"
Vertical . .	145–154	"	Mature	3.80	8.00	13.0	Groedel.
" . .	165–174	"	"	4.00	8.10	13.2	"
" . .	145–154	"	Immature	3.10	7.00	11.2	"
" . .	165–174	"	"	4.10	7.00	11.8	"
Horizontal . .	111–120	..	Children	2.90	6.35	9.9	Verth.
" . .	121–130	..	"	3.60	6.90	10.6	"
" . .	131–140	..	"	3.30	6.90	10.9	"
Vertical . .	111–120	..	"	2.85	5.97	9.3	"
" . .	121–130	..	"	3.04	6.35	10.1	"
" . .	131–130	..	"	3.08	6.79	10.9	"

Recently, Bardeen, Cohn, Smith and others have again compared the values of normal civilians with those obtained from soldiers. The following table given by Smith indicates the relation of the different diameters to weight and height.

COMPARISON OF DIAMETERS AND AREA WITH THE DIETLEN AND BARDEEN NORMALS.

Weight, kg.	Soldiers.				Dietlen table.				Bardeen table.	
	Cases.	T.D., cm.	L.D., cm	Area, cm.	Cases.	T.D., cm.	L.D., cm.	Area, sq. cm.	T.D., cm.	Area, sq. cm.
55 to 59 . .	40	12.5	13.6	111	39	12.9	14.0	112	12.4	110
60 to 64 . .	82	12.1	13.9	113	54	13.1	14.1	114	12.7	116
65 to 69 . .	61	13.1	14.1	118	24	13.2	14.5	118	13.0	121
70 to 74 . .	50	13.5	14.6	127	18	13.4	14.8	122	13.4	128
75 to 79 . .	35	13.7	14.5	131	5	14.3	15.5	131	13.7	124
80 to 84 . .	9	13.7	14.7	135	5	14.4	15.3	133	14.0	140

MEASUREMENTS COMPARED BY HEIGHT WITH DIETLEN'S NORMALS.

Height, cm.	Soldiers.						Dietlen's normals.					
	Cases.	M.L., cm.	M.R., cm.	L.D., cm.	B.D., cm.	Area, sq.cm.	Cases.	M.L., cm.	M.R., cm.	L.D., cm.	B.D., cm.	Area, sq.cm.
155–164 . .	18	4.0	8.3	13.3	9.9	111	72	4.1	8.7	13.8	9.9	109
165–174 . .	174	4.1	8.5	13.1	10.2	118	77	4.2	8.8	14.1	10.3	116
175–187 . .	185	4.3	8.7	14.2	10.7	122	29	4.4	9.1	14.8	10.7	127

In general, such tables show that there is an increase in the heart as well as in the long and transverse diameters, as weight and height increase.

A consideration of extensive tabulations of actual measurements made by Smith, Cohn, Schieffer, Dietlen, Groedel and others indicates that the variations in normal individuals do not usually deviate from the values calculated from Bardeen's formulæ by more than about 10 per cent. (For detailed method employed by the U. S. Army in evaluating measurements as regards both weight and height, *cf. U. S. Army Roentgen Ray Manual*, p. 412.)

CLINICAL SIGNIFICANCE OF ROENTGEN-RAY EXAMINATION.

Combined fluoroscopic, radiographic and orthodiagraphic examinations of diseased conditions give evidence of the nature of the affection through the occurrence of changes in: (*a*) The character of the pulsation; (*b*) the position of the heart; (*c*) the size and form of its outline.

In fluoroscopic examinations the *lower right border* (right auricle) expands extensively during systole in some cases of tricuspid regurgitation. The *upper left border* (aorta) gives strong systolic expansions in aortic insufficiency. Whenever the pulsations of the left auricle become visible, as in mitral lesions, they are differentiated by being presystolic in time. Strong pulsations of the pulmonary artery are evident on the left side in cases of persistent ductus arteriosus; or, more frequently, when a severe stasis due to mitral lesions is present. They have been observed when an aneurysm ruptures into the pulmonary artery, but this event is rare. Abnormal rhythms, as heart-block and pulsus alternans, have been studied and diagnosed by fluoroscopic methods, but this procedure possesses no obvious advantages over auscultation.

A *change in the position of the heart* may occur: (*a*) From congenital causes, as situs inversus vicerum; (*b*) from pleural and pericardial adhesions; (*c*) from changes in the intrathoracic volume. These last are very common. Even normal variations are caused by the vary-

ing position of the diaphragm. In long-chested individuals the cardiac shadow is long and narrow, the axis being more vertical, while in short-chested individuals or in those in whom the diaphragm is pushed up by abdominal distention, it is broad and assumes a more horizontal axis. Its position changes as the diaphragm ascends and descends in respiration. It should be remembered that normally the heart is subject to considerable shifting and undue weight should not be attached to slight variations in position. If, for any pathological cause (*e. g.*, enlargement of the liver), the right dome of the diaphragm is pushed upward, the heart shadow will be displaced to the left. Pulmonary affections, such as atelectasis, tuberculosis and pneumothorax, cause a traction on the heart toward the side of the lesion. On the contrary, pleural effusions, tumors, etc., push the heart toward the opposite side.

Changes in the size of the heart shadow or orthodiagram when sufficiently marked to be safely beyond the limits of normal variation are of the greatest practical importance when obtained by guarded technic. The heart shadow probably decreases whenever the heart accelerates (*e. g.*, in exercise, tachycardia, after atropine), although the results obtained concerning this point have been discordant. During asthmatic attacks, the heart is also reduced in size. A condition simulating asthma, as far as the effect upon circulation is concerned, can be produced by the well-known experiment of Valsalva, which consists in taking a deep inspiration and then, with closed glottis, making a forced expiration. This diminishes the blood content of the heart, which accounts for its decreased size. In tuberculosis the shadow is decreased, and here it is often assigned, but without good reasons, to an actual hypoplasia of the heart muscle.

The heart outline increases after continued hard labor or exercise, pathologically also in nephritis and arteriosclerosis. In these cases an actual hypertrophy, resulting from the greater strain to which the heart has been continually subjected, is usually the cause. The increase in size (often temporary) associated with acute infections, such as diphtheria, scarlet fever and polyarthritis, is no doubt accounted for by a dilatation of the heart.

The details of the enlargement are of the greatest importance in heart lesions, in which case it is due either to dilatation or to hypertrophy and hence accompanies only lesions of considerable duration and severity. The nature of the dilatation or hypertrophy determines the direction of the enlargement and the contour of the shadow. A left ventricular enlargement takes place to the left. Dilatation or hypertrophy of the right ventricle displaces the shadow partly to the right but also, to a marked degree, upward and to the left. In typical cases of *aortic insufficiency,* the heart shadow is enormously increased toward the left and the contour resembles a horizontal oval or is sometimes called "shoe-shaped" (Fig. 184). The aortic shadow

is increased in width and the apex is never merged with the shadow of the diaphragm. *Aortic stenosis* causes very similar though less pronounced changes in the roentgenographic outline. In *mitral stenosis* the heart shadow, which is relatively small, resembles more nearly a vertical oval. The enlarged left auricle becomes prominent on the left margin (Fig. 179) and above it the pulmonary artery bulges, thus giving the entire left border a step-like appearance. In *mitral insufficiency* (Fig. 178), the enlargement tends to be uniform in all directions, giving the shadow the appearance of a poorly rounded circle. The right auricular border is distinctly enlarged to the right and the pulmonary artery dilated. The left ventricular shadow is increased toward the left.

Aside from its service in the diagnosis of cardiac affections, the roentgen ray has given valuable information concerning extracardial conditions, as pericardial effusions, aneurysms, etc., which will be discussed in chapters dealing with these conditions.

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SECTION III.

DISEASES OF THE HEART AND CIRCULATION.

CHAPTER XX.

FUNCTIONAL DISTURBANCES OF THE HEART AND CIRCULATION.

It is the fundamental function of the heart to ensure at all times a capillary blood flow that is adequate to meet the nutritional and respiratory demands of the body cells. When, for any reason, these demands are increased as a result of agumented metabolism or when the composition of the blood is so altered as to jeopardize these needs, it becomes the function of the heart to increase the minute flow through its adaptive power. The fundamental mechanisms through which this is accomplished are not developed to equal degree in different individuals, however, and, in consequence, the reactions are in one case distinctly physiological in nature and in the other more apt to border upon the pathological. Thus, it happens that in reaction to such influences as exercise, changes in barometric pressure, extremes of external temperature, etc., an occasional heart fails to meet the test and gives rise to the so-called functional disturbances.

It is quite clear, therefore, that in order to evaluate the pathological physiology of such reactions, it is necessary at all times to compare them with the average run of individuals which are arbitrarily designated as the "normal."

THE CIRCULATORY REACTIONS IN MUSCULAR EXERCISE.

During muscular exercise, the oxygen requirements of the body are increased almost in direct proportion to the external work performed. Not only the consumption of oxygen per minute but also its utilization during the interval of separate pulse beats, *i. e.*, the oxygen pulse, increases (Henderson and Prince). While the attendant changes in blood CO_2 and H-ion concentration results in an increased pulmonary ventilation which makes a larger supply of oxygen available in the lung alveoli, it is obvious that this can be of no avail unless the minute flow through the muscle capillaries is also increased.

By the use of gasometric methods, it has been shown conclusively that this occurs partly as a result of an increased minute discharge of the ventricles (Plesch, Krogh and Lindhard, Christiansen, Douglas and Haldane, etc.). This may obviously be accomplished in either or both of two ways, viz.: By an increased heart rate or by an increased systolic discharge. That an increased heart rate occurs during exercise is a matter of general observation. The earlier work (Krogh and Lindhard) indicated, however, that the systolic discharge is at the same time greatly augmented, being more than doubled in strenuous work. More recent investigations by improved methods (Boothby, Douglas and Haldane) indicate, however, that while there is a considerable increase in systolic discharge in most individuals, it is not as great as the earlier observations led us to believe. Probably the most important point brought out by recent work is that considerable variation exists in different individuals as regards the effect of exercise on systolic discharge. Thus, in 3 cases carefully studied by Douglas and Haldane, the systolic discharge was more than doubled in one, appreciably augmented in a second, but remained unchanged in a third. A result similar to the last is also reported by Henderson. In 17 students studied by the Roentgen-ray method, Meek and Eyster found the systolic discharge increased to varying degree in 14, but somewhat decreased in 3 cases. In 4 of the 14 cases, the heart rate increased by about 10 beats per minute, the increased systolic discharge accounting largely for the great increase in minute volume. The further observation of Douglas and Haldane—that the individuals showing a great increase in systolic discharge had a much higher oxygen utilization at rest than the individual showing no increase—may be of significance as to the cause of such variations.

The Mechanism of Increased Systolic Discharge.—The ways in which systolic discharge may be augmented in spite of an increased heart rate and an abbreviated filling phase of diastole has already been analyzed (*cf.* page 106). Two mechanisms may be thought of: (*a*) An increased venous pressure, and (*b*) decreased ventricular tonus. We have already registered our opinion that while a variable state of tonus is possible or probable, its operation as a compensatory factor has not yet been established in a crucial way (*cf.* page 120). It is clearly impossible, therefore, to evaluate the possible rôle that changes in tonus may play in exercise. We know, however, that the venous pressure augments (Hooker); we know also that this causes a more rapid diastolic inflow and a larger and more rapid systolic discharge (Patterson, Piper and Starling, Straub, Wiggers and Katz). During exercise more blood is squeezed from the muscles into the veins, and this is the more effective as the supplying arterial pressure is augmented and the amount of blood within the muscle capillaries during relaxation is much increased, owing to the opening up of dormant capillaries (Krogh). To this muscular pumping mechan-

ism must be added the possible diversion of blood from the liver and internal organs, owing to the vasoconstriction of the visceral arterioles as well as the pressor influence of the deepened respiration.

The increase in systolic discharge thus occasioned by equivalent degrees of diastolic distention varies greatly in different individuals, however. This depends to a considerable degree upon the inherent properties of the cardiac muscle to respond. A "good" heart will cause a considerably increased systolic discharge with slight augmentation of diastolic volume; a "poor" heart requires a much greater distention in order to give the same increase in systolic discharge (Patterson, Piper and Starling). Many fundamental factors, of course, determine the inherent condition of cardiac muscle, *e. g.*, the quality and quantity of its blood supply, chemical and toxic influences acting directly upon the heart muscle, etc. In normal hearts, however, it practically sifts down to the question of previous training or lack of training. On this basis we are able to explain why in trained individuals the increased minute volume during exercise is accomplished more largely by increased systolic discharge, whereas in the untrained normal individuals the systolic discharge increases relatively little and the entire increase in minute volume is accomplished by cardio-acceleration (Krogh and Lindhard). It is not unreasonable to proceed a step farther and suppose that in men, as in experimental animals, we occasionally meet a heart muscle so depressed by toxic or possibly nervous influences that it is quite incapable of responding by any augmentation of discharge to such an increased venous return. When this happens, the heart dilates and the entire burden of maintaining the increased peripheral minute volume must then be assumed by an excessive increase in heart rate. When this in turn fails, because the systolic volume is actually reduced as a function of heart rate, pathological functional disturbances occur. We have here a physiological picture of the borderland cases merging gradually into those which must be considered distinctly pathological. It is obvious that this interpretation of the cardiac response necessitates the assumption that an increase in diastolic volume of the heart occurs during exercise. This has generally been regarded as contrary to the majority of observations of the heart by means of the roentgen rays, all of which indicate that if any change takes place it is a decrease in the shadow of the heart (Moritz, Dietlen, Hoffmann, de la Camp). As Bainbridge justly points out, however, account must be taken of the fact that these observations were made immediately after and not during exercise, *i. e.*, at a time when the major factor responsible for increased venous return (*i. e.*, muscular contraction) no longer operates. In observations made during exercise an actual though small increase in the size of the heart has been reported by Nicolai and Zuntz. More recent investigations indicate, however, that there is

considerable variation in the diastolic volumes in different individuals. Thus, Williamson found that the diastolic size decreased in 29 cases, increased in only 3, and remained unaltered in another. Bruns and Roemer found in 46 individuals studied, an increase in diastolic size in 15 per cent, a decrease in 25 per cent, while in the remaining 60 per cent increase and decrease alternated. Meek and Eyster found in 17 subjects in whom both systolic and diastolic volumes of the same heart cycle were studied, an increase in diastolic size in 10 and a decrease in 7 during muscular exercise. Of greater significance was the further observations that in 6 cases in which the diastolic volumes were smaller, the systolic discharge was augmented. Such observations, therefore, indicate that during exercise, as in animal experiments, an increased diastolic volume is not absolutely necessary in order to have the systolic discharge augmented.

How are such effects produced? While it is possible that tonus changes may be concerned, it is quite possible to explain these changes as combinations of heart-rate and venous-pressure effects. Indeed, the conditions obtaining in exercise are probably somewhat similar to those obtaining in animals from which the volume curves of Fig. 31 were recorded. As long as the heart rate does not alter materially, each increase in venous pressure causes concomitant increases both in diastolic volume and systolic discharge (lower series of segments, Fig. 31); when, however, the heart rate also increases (upper series, Fig. 31) then the diastolic size decreases and in spite of this the systolic discharge may remain unaltered (*cf. D* and *E*, upper series). Furthermore, although the diastolic volume of the heart in segment *E* is slightly less than in segment *C*, yet the systolic discharge is much increased. As the only variable is the higher venous pressure, we must conclude that the initial tension is also increased. Meek and Eyster's conclusion, viz., that the initial tension rather than the diastolic volume determines the systolic discharge, therefore, receives experimental support.

The Mechanism of Cardiac Acceleration.—Since cardiac acceleration is always a pronounced factor in the establishment of increased minute volume during exercise, and in unresponsive hearts may indeed become the sole factor, it is important to analyze the mechanism through which such acceleration is invoked and to discuss why it may fail to maintain an adequate circulation.

The sequential changes in heart rate during exercise have been most thoroughly studied by Bowen. This investigator found that the heart rate increases immediately after exercise has begun. It continues to increase progressively from ten to twenty minutes and then becomes constant. As exercise is continued a secondary gradual rise in rate follows. Contrary to expectations, however, the results of Bowen showed that systole is slightly lengthened during the early increase in heart rate, the quickening of the heart being entirely

produced by shortening of diastole. Only during the secondary increase does the systole actually shorten.

The significance of these results which were not fully appreciated at the time now seems quite clear: Rapid acceleration of the heart, such as occurs from the removal of vagus influence alone, invariably leads to a reduction in duration of systole. Combined with a simultaneously increased venous pressure, however, which tends to lengthen the duration of contraction, this influence dominates. Such results, therefore, give almost unmistakable evidence of an early increase in venous return and presumably an increased systolic discharge. Gradually, however, systole shortens again and below the normal range. Gasser and Meek have shown that the early increase in heart rate after exercise occurs also in animals with both vagi cut and adrenals removed, indicating that the accelerator mechanism is also involved in the cardiac acceleration. Now it has recently been shown that this operates very decidedly to abridge systole and, accordingly, it is easy to account for the subsequent diminution of systole as the heart continues to accelerate during exercise.

The secondary increase in heart rate is more difficult to interpret. Among the possibilities suggested are: (1) The entrance of increased amounts of adrenalin into the blood;[1] (2) increase in body temperature; (3) changes in the H-ion concentration; (4) reflexes due to increased venous pressure (*cf.* page 144).

The Peripheral Mechanisms in Exercise.—In addition to the increased minute discharge of the heart the capillary blood flow through the muscles is also aided by a number of peripheral mechanisms. It has been clearly demonstrated that muscular contraction produced by stimulation of motor nerves increases the blood flow through muscles independently of the supplying pressure (Gaskell, Chauveau and Kauffmann). This may be due to a vasodilatation mediated either through nervous channels or more probably through chemical effects of tissue metabolism (*e. g.*, lactic acid). Furthermore, new capillaries are apparently opened up within the tissues either as a result of a deficiency of oxygen, a local increase in H-ion concentration or hormonal effect of tissue metabolites (Krogh, Dale and Richards). Finally, the mechanical effect of muscular contraction, by means of which increased amounts of blood are actually propelled through the acting muscle, must not be left out of consideration (*cf.* page 148). In addition to these peripheral mechanisms within the muscles themselves, it has been generally supposed that a constriction of the splanchnic vessels occurs and diverts larger volumes of blood from the viscera to the skin and muscles. While there is some evidence that the size of the internal organs decrease during exercise, it has by no means been demonstrated conclusively

[1] *Cf.* Hartman, Waite and McCordock.

whether this diversion from the viscera is due to an active constriction of the splanchnic vessels or whether it occurs mechanically as a result of the development of paths of least resistance through the contracting muscle and the dilated skin vessels. The idea that an active and intense vasoconstriction of the splanchnic vessels occurs can, therefore, only be regarded as an attractive though as yet unproven hypothesis.

Changes in Arterial Blood-pressure.—The effect of exercise on the arterial blood-pressure is the resultant of the increased cardiac discharge and increased heart rate on the one hand and of the increased peripheral flow to the muscles and skin on the other. These reactions during and after exercise have been studied by many investigators (L. Hill, Bowen, Lowsley, Pembrey and Todd, Cotton, Lewis and Rapport, etc.). In normal individuals there is a rapid rise of systolic pressure at the very beginning of exercise, which is followed by a more gradual increase to a maximum within five to twenty-five minutes. The actual rise depends upon the degree and length of exertion and may reach some 60 or 70 mm. (Bowen, Lowsley). The diastolic pressure also rises but not quite so much as the systolic, a maximum increase of 40 mm. being found in some individuals. The pulse pressure increases from 10 to 30 mm. As fatigue comes on the systolic pressure declines somewhat, though the diastolic pressure may not be so affected.

Immediately after the cessation of exercise the blood-pressure falls quickly but not so rapidly as the primary fall in pulse rate (Bowen). In many cases it declines to subnormal levels, which is followed by a rise reaching a maximum from twenty to sixty seconds, after which it more gradually falls again to normal within one to four minutes after the cessation of exercise. It is obvious, therefore, that the reaction of the blood-pressure to exercise cannot be studied by taking blood-pressures immediately or some time after exercise has been carried out. The immediate decrease in blood-pressure after the cessation of exercise has been interpreted as due to the sudden decrease in the venous return, when the pumping action of the muscles ceases. The subsequent rise and gradual return to normal are accounted for by the continued acceleration of the heart and an adaptive peripheral vasoconstriction in the muscles.

The Physiological Syndrome of Effort.—When a "normal" individual undergoes a strenuous or prolonged physical exertion he becomes conscious, first of all, of certain compensatory functions, called into play. He is aware of the deeper respirations and breathlessness as well as the rapid heart action or palpitation. If the demands of the tissues for increased blood flow during strenuous exercise are not quite met, other symptoms result, such as giddiness or faintness, sensations of fatigue or exhaustion, tight sensations or pains in the chest, etc. After the cessation of exercise, aching limbs,

tremors, general exhaustion are followed by muscular stiffness, lassitude, etc. This symptom-complex following vigorous exercise in normal individuals has been termed the "physiological syndrome of effort." (Lewis.)

EFFORT SYNDROME—IRRITABLE HEART—NEUROCIRCULATORY ASTHENIA.

Nomenclature.—While the signs and symptoms constituting the "effort syndrome" appear in healthy individuals only after prolonged and vigorous exercise, they occur after comparatively mild forms of exertion in another class of individuals. Such persons, as a rule, elect occupations which involve little or no physical effort, and under these conditions remain in apparently perfect health. When they indulge in more strenuous exercise or change to occupations involving greater exertion, however, they develop the effort syndrome in so pronounced a form as to suggest a definite circulatory malady. Such cases only occasionally come to the attention of physicians in civil practice, but are exceedingly common under war conditions, where it is brought out by the greater exertion of army training or is aggravated by the psychoneuroses developing in war life. While this symptom-complex had no doubt been previously recognized as a serious menace in army life, the first clear account of its incapacitating influence was given at the time of our Civil War by Hartshorne and later in more amplified form by Da Costa (1871), who designated the malady as the "irritable heart of soldiers." Since that time the condition has been variously known as soldier's heart, irritable heart, cardiac neurosis, disordered action of the heart (D. A. H.), neurocirculatory asthenia (N. C. A.), etc., but following the suggestion of Lewis, has in later years been referred to as *effort syndrome*. In suggesting this term, Lewis sought less to supply an equivalent or better term descriptive of the clinical diagnosis than to substitute a term descriptive of the symptomatology regardless of the pathological condition to which it is due.

"The difference in symptomatology which exists between health and this form of ill health is largely a difference in degree; the gauge is the amount of work which, performed in a given space of time, will provoke the symptoms. Symptoms produced in normal subjects by excessive work are produced in the patients by lesser amounts; the smaller amount of work required, the more severe the malady. Naturally, there is no sharp line of division; there is in a large group of patients a perfect grading from the healthy man to him who is seriously unwell. We are traveling in the borderland between health and disease. This point of view has its value; it directs investigation toward the normal reactions of the body to exercise and to the corresponding reactions in disease; it brings us to inquire into the reserves

of some of the most important bodily functions, and into the manner in which these reserves are reduced." (Lewis.)

It is obvious that thus used there is nothing pathognomonic in the effort syndrome, nor does it necessarily predicate a primary cardiac disturbance. Effort syndrome is a characteristic of a large variety of well-established pathological conditions; it occurs, for example: (1) In chronic valvular and myocardial disease; (2) during and after acute infections; (3) in thyrotoxicosis; (4) in early tuberculosis; (5) in damage to the pulmonary epithelium, as in "gassing;" (6) in diseases associated with disturbance of the alkali reserve of the blood or oxygen deficiency.

In his stricter application, Lewis limited the term "effort syndrome" entirely to such cases in which responsible causes could not be established—in other words, he employed the unqualified term as synonymous with *effort syndrome of unknown origin.*

While this term has served so many useful purposes during the World War that its general adoption in preference to others suggestive of definite pathological conditions is to be commended, its double significance had the unfortunate effect that very different types of cases have come to be included in the category of effort syndrome by different medical men. With the great experience gained by the late war in transferring cases of effort syndrome from groups of unknown to those of known origin, it leaves relatively fewer cases in the former group, and it would now seem wise, for descriptive purposes at least, to designate these cases of unknown origin by some other distinctive name. Possibly the term "irritable heart," though clearly a misnomer, is still the best that we can apply to this condition. The suggestion that they be referred to as neurocirculatory asthenia leaves out of consideration the fact that certain cases of "effort syndrome" are obviously not accompanied by psychoneuroses. Since, as we shall later see, all of these cases come under the class of depressed myocardium, the term "myocardial asthenia" covers all of those forms of effort syndrome which still remain obscure in their origin.

When considered on the basis of their personal history and the examination of other body functions, such cases of myocardial asthenia fall again into several classes: (*a*) Cases in which the onset of the affection dates from some remote antecedent infection or intoxication; (*b*) cases in which there is a general constitutional inferiority dating from, or it may be more properly said, before birth; (*c*) cases in which the cardiac symptoms are associated with or a part of a general psychoneurosis. The last and possibly the last two types—which greatly predominate—may well be designated by the term neurocirculatory asthenia.

Clinical Manifestations of Myocardial Asthenia (Irritable Heart, Neurocirculatory Asthenia).—The chief symptoms of which indi-

viduals of this class complain are, in the order of their frequency, pains in the chest, shortness of breath, fatigue, giddiness, palpitation, precordial pain and tenderness and fainting attacks. Malaise, lassitude, insomnia, troubled dreams, etc., are frequently added complaints. On examination, the extremities are found to be cold and clammy and sometimes blue, beads of sweat stand in the axilla, the skin is often mottled or cyanotic and the face presents a drawn or anxious appearance. Coarse tremors of the extremities and areas of hyperesthesia over the breast are common.

Physical examination of the cardiovascular system usually reveals a rapid pulse (80 to 130 per minute) and a vigorous apex beat. The cardiac area on percussion is not enlarged. The systolic murmurs and thrills often present have been shown to be of no pathological significance (Cohn, King, etc.) (*cf.* also page 546).

Careful studies by instrumental methods have revealed no further abnormalities of the circulation. Blood-pressure is usually normal at rest (Rapport, Sturgis), but like the pulse rate is subject to sudden variations as a result of mental disturbances or mild exercise. The teleroentgenogram or orthodiagram have shown that the hearts are not often enlarged, but, on the contrary, are frequently smaller than normal (Meakins and Gunson, Smith). The electrocardiograms show no disturbances of conduction, and arrhythmias are no more frequent than in normal individuals (Clough). The vital capacity, the composition of alveolar air and the alkali reserve of the blood are normal (Adams and Sturgis, Drury, Levine and Wilson, Wilson, Levine and Edgar), the thyroid gland is not overactive for the basal metabolism is usually not increased (Tompkins, Sturgis and Wearn). Cases which show an increased metabolism should not be included in our classification of myocardial asthenia. In some individuals with cold, bluish extremities the capillary pressures have been found increased, but the peripheral venous pressures are normal (Briscoe).

Clinical Physiology.—In view of these many negative findings, many attractive hypotheses advanced to explain these conditions must now be considered as merely of historical interest, for they are completely disproven and it is necessary to consider only those hypotheses which regard the cardiac phenomena as associated either with a hyperexcitable sympathetic system or with a depression or diminished functional capacity of the ventricular myocardium. The application of known physiological facts to the analysis of these cases makes it extremely probable that a combination of these two conditions exists in different proportions in different individuals and explains all the abnormal circulatory phenomena.

Many evidences, both clinical and experimental, point to the existence of a hyperexcitable accelerator mechanism. The rapid and, at the same time, forcible ventricular beat is thus readily explained, as is also the ready increase in heart rate following emotional or

reflex stimuli. Such individuals, furthermore, show a prompt acceleration, due to exercise, when the vagus influence has previously been abolished by atropine (Cotton, Rapport and Lewis), indicating that the upset in balance between vagus and accelerator influence during rest is accounted for, not by a reduced vagus influence, but rather by an increased accelerator tonus. Furthermore, some, though by no means all, show an increased response to epinephrin as far as cardiac acceleration is concerned, even when this causes no abnormal augmentation of general metabolism (Wearn and Sturgis). Not in accord with this view, on the other hand, is the fact that the duration of systole is not shorter than at equivalent rates in normal men (*cf.* page 204), as would be anticipated if an augmented accelerator tone existed; but, on the contrary, the duration of systole is actually longer (Wiggers and Clough). Finally, many subjects during rest do not show an accelerated heart rate.

While an augmented accelerator activity may be responsible for the rapid "resting heart" when it occurs, as well as the attendant vigorous ventricular action, while it may also account for sudden palpitation developing as a result of psychic or reflex stimuli, *it is not at all clear how such a mechanism can explain the effort syndrome following moderate exercise.* Accelerator nerve stimulation results not only in an increased heart rate but also in an increased systolic discharge. Assuming that the accelerator mechanism is more readily stimulated in these conditions after exercise we should anticipate the delivery of greater minute volumes and not diminished minute volumes, such as are apparently indicated by the symptoms of giddiness and actual fainting. In other words, such a mechanism might be supposed to be favorable rather than unfavorable as regards the reaction of the heart to exercise. While it cannot, of course, be said that such a mechanism is not concerned in the response to exercise, we must suppose that some other reaction is fundamentally responsible for the effort syndrome.

A much more plausible explanation of the effects of exercise on the heart and circulation in these conditions is afforded by the supposition that a fundamental depression of the myocardium continually exists. This may be due: (*a*) To a constitutional inferiority of the heart muscle; (*b*) to the permanent effect of some antecedent infection or metabolic disturbance; (*c*) to functional or anatomical abnormalities in the blood supply of the heart. The possibility that it may be induced by direct nervous mechanisms is contrary to physiological evidence. The vagus nerves, as far as we know, do not reach the ventricular muscle and the accelerator nerves exert a tonic rather than depressing influence on ventricular irritability.

While the idea that a functionally weakened myocardium is at the foundation of the cardiovascular complex has been frequently suggested by clinicians, only recently has it been possible, how-

ever, to formulate a physiological conception as to how this operates to decrease the adaptability of the heart during exercise and strain (Starling and associates, Bainbridge). The chief characteristics of a depressed ventricle are: (1) Its inability to react to increasing venous return with larger systolic discharge, and (2) a smaller output than normal at equivalent initial pressure, and diastolic volumes. Applying these experimental facts it is conceivable that, supplied with the same venous return at rest, the depressed myocardium ejects correspondingly smaller volumes. To compensate for this, *i. e.*, to meet the requirements of the tissues at rest, an increased heart rate results reflexly. When an increased demand for oxygenated blood arises during exercise, the increasing venous return is not able, as normally, to increase the systolic discharge, and the accelerator mechanisms already overtaxed are not able to increase the minute volume sufficiently. In short, under such conditions increased rate alone supplies the needs of the tissues but only for comparatively moderate forms of activity. When this is exceeded disturbed blood-pressure and disturbed blood-gas relations lead to the same effects as occur normally when the capacity of the heart is exceeded after the most strenuous exercise.

THE EFFECTS OF HIGH ALTITUDE.

Symptomatology.—The acute effects of a rather rapid decrease in barometric pressure are due entirely to the anoxemia of the various tissues, and the so-called symptoms of *altitude sickness* are either due to primary effects of oxygen lack (Bert, Mosso, Douglas, Haldane, Henderson and Schneider), particularly on the central nervous system, or to the compensatory mechanisms of the respiration and circulation, through which an increased supply of oxygen to the body cells is attempted. When individuals adapted to a life at or near sea level ascend to higher altitudes, an altitude level is reached which may be called "critical" for each individual in the sense that it gives rise to an acute form of "mountain sickness" or "altitude sickness." Buzzing in the ears, dimmed vision, nausea, vomiting, great prostration, insomnia, dizziness or actual fainting are among the common symptoms. The skin is of a vivid blue color and the pulse is very rapid. In more rapid decreases of barometric pressures, as in airplane ascent, the subject at critical levels may be said to pass through the following states: (1) Decrease and loss of attention; (2) loss of voluntary muscular control; (3) complete unconsciousness. The critical altitude level at which these symptoms occur varies for different individuals; some developed symptoms at less than 10,000 feet, others escape up to an elevation of 14,000 to 17,000, while it is the rare individual who is able to resist the effects of more than 18,000 feet.

Even at elevations below the critical level, the ability of performing muscular exercise is very much abridged or entirely abolished. Consequently, the circulatory effects of exercise complicate the effects of altitude change when the ascent is accomplished by the physical effort of mountain-climbing. The pure effects of altitude change can only be studied when the ascent is made passively, as by railway, motor conveyance or airplane. Since the symptoms are entirely due to oxygen lack, it is possible to reduplicate the effects in laboratories either by allowing individuals to rebreathe into an apparatus in which CO_2 is absorbed or in which dilute mixtures of oxygen are breathed. Finally, it is possible to place an individual in decompression chambers in which the barometric pressure is artificially reduced at varying rates.

The Cardiovascular Effects.—Inasmuch as there is a general impression that the effect of low barometric pressure exerts a deleterious effect upon the heart and circulation, it may at once be pertinent to inquire what the circulatory changes are and to what extent they are responsible for the symptoms. Careful observations of the circulation made in the Pike's Peak expedition of 1911 (Douglas, Haldane, Henderson and Schneider) have shown that the circulatory effects are not very pronounced when the ascent of mountains is made passively to elevations below the critical level. The heart rate and blood-pressure remain practically normal at first, but for several days after reaching a high altitude and sometimes even for a week or two a gradual and progressive cardiac acceleration occurs when the subject remains at rest. The degree of cardiac acceleration is determined, to a considerable extent, by physical fitness, being greater in persons already leading sedentary lives and unaccustomed to regular exercise. The venous pressure decreases somewhat, but the capillary pressure remains unaltered (Schneider and Sisco). Since the product of the pulse pressure and heart rate increases and the blood flow through the hands is augmented, Schneider and Sisco concluded that the minute volume of the blood increases. Since it has been found, however, by gasometric methods applied both to man (Hasselbalch and Lindhard) as well as in experimental animals (Doi) that the minute volume is apparently unchanged during exposure to low-oxygen tensions, it must be concluded that the increased peripheral capillary flow, of which the results of Schneider and Sisco are criteria, is determined largely by the peripheral relaxation of vessels.

If the mountain ascent is made to levels above that critical for any individual, a further acceleration of the heart and an increase in arterial pressure occurs as the symptoms of altitude sickness develop.

Upon physical exertion at subcritical elevations, the heart accelerates greatly, while the systolic and diastolic pressures fall somewhat. Extreme weakness, exhaustion, dizziness and fainting then readily result.

It may logically be supposed that the effects of altitude change encountered in aviation may possibly differ, owing to the fact that the changes in barometric pressure occur more rapidly and that the duration of exposure is considerably shorter. A careful study of this question has been made at the Medical Research Laboratories at Mineola. It was found that no essential differences occurred. After short exposure to decreased oxygen pressures, such as the aviator experiences, the compensatory mechanisms are almost entirely limited to the respiration and circulation (*cf.* also page 584). Very few persons benefit by an increased hemoglobin concentration or a possible secretory activity of the pulmonary epithelium, such as has been supposed to be demonstrated during continued life at higher altitudes. In fact, with a progressive decrease in O_2 pressure, the increased respiratory movements cannot compensate by increasing the alveolar O_2 percentage, as is the case in exercise at sea levels. The changes in the circulation during rapid oxygen deprivation, similar to that occurring in aviation, may be summarized as follows: The heart accelerates slightly and gradually in the early stages of pressure reduction, becomes more pronounced when the oxygen percentage falls to 15 or 12 and very profound at the lowest endurance of the individual, *i. e.*, when he breathes mixtures of 7 or 6 per cent of oxygen. In general, it was found that the more rapid the rate of oxygen reduction the lower the final percentage of oxygen that could be tolerated before unconsciousness developed. The blood-pressure changes are apparently somewhat variable (Corbett and Bazett, Lutz and Schneider, *Mineola Laboratory Manual*). As a rule the systolic pressure remains unchanged, but, in about one-quarter of the cases examined, a slight rise occurs early in the experiment. The diastolic pressure gradually decreases by 4 to 8 mm. The pulse pressure is largely determined by changes in diastolic pressure, being, as a rule, increased. Again, an increased flow through the tissue capillaries is demonstrated by the increased product of the pulse pressure and heart rate.

When so low a level of oxygen deficiency is reached that the circulation can no longer respond by increased rates, *circulatory failure* supervenes. This is initiated by a fall of diastolic pressure, soon followed by a fall of systolic pressure as well. The heart sounds become more feeble and, according to the Mineola investigators, the heart then dilates. Such a dilatation could not be confirmed by Le Wald and Turrell, however, by roentgenographic methods. When this circulatory crisis is reached the skin is of an ashy pallor, cold sweat stands out over the body and there is loss of muscle tone so that the patient falls from his seat.

The time at which such a circulatory crisis begins to develop varies in different individuals. In some, the reduction in oxygen tension may be carried to the point of unconsciousness without evidence of

circulatory failure; in others it develops relatively early and is the cause of the fainting attack. Three types of cases were recognized among prospective aviators at Mineola: "(1) The optimum, in which the pulse rate accelerates moderately as the oxygen decreases, the systolic pressure is unchanged or shows a terminal rise of not more than 20 to 30 mm. Hg., and the diastolic pressure remains unchanged or rises slightly. (2) The controlled diastolic fall, in which the pulse rate accelerated moderately and the systolic pressure rises as the diastolic pressure gradually falls. (3) The fainting type, in which after a period of fair, good or excessive response in the rate of heart beats to low oxygen the diastolic pressure suddenly falls, and soon thereafter the systolic pressure falls and the pulse rate slows. The optimum type may tolerate as low an oxygen as 6 per cent and may lose consciousness without fainting. He recovers quickly when restored to air, while the heart rate and blood-pressures are soon back to their normals. The fainting type rarely endures as low an oxygen, and if allowed to run his course faints completely, and as he revives he requires a considerable time, sometimes an hour or two, to regain his normal pulse rate and blood-pressures. There are, of course, gradations between the types here described."

The pulse pressure during a rebreathing test remains fairly constant in most men until the oxygen has fallen to between 12 and 9 per cent (14,500 to 22,000 feet), after which it increases in amount during the further reduction in oxygen. The rise in pulse pressure occurs when the systolic pressure is rising and the diastolic is either remaining constant or slowly falling. This is also the period when the heart beat is accelerating most rapidly.

Clinical Physiology.—At increasingly high altitudes the partial pressure of oxygen is reduced and, consequently, the oxygen pressure in the arterial and capillary blood is decreased. This has the effect of reducing the oxygen diffusion into the body cells and leads to disturbances in their function, affecting particularly the cells of the central nervous system. In brief periods of exposure, this tendency is counteracted largely by the increase in the minute volume flowing through the capillaries. The reactions above noted indicate that this is accomplished by a moderate cardiac acceleration together with a relaxation of the peripheral arterioles and, possibly, also by the reaction of local capillary mechanisms. There is no evidence in man that a compensatory increase in systolic discharge, due to an increased venous return, operates as in exercise, nor is there evidence that ventricular discharge is affected by accelerator nerve action. Animal experiments (Doi), in fact, indicate that the systolic discharge is decreased as the heart rate accelerates. The most remarkable feature, corroborated also in animal experiments (Greene and Gilbert) is the relative stability of the systolic and diastolic pressures over considerable ranges in O_2 decrease. This tends to indicate that

the tendency for increased heart rate to augment the arterial pressure is nicely counterbalanced by a reciprocal reduction in the peripheral resistance. The Mineola investigators also point out that there is probably a further compensatory vascular reaction, by virtue of which larger quantities of blood are directed from the viscera and inactive muscles by means of vasoconstriction to the more vital organs, such as the brain and heart. As these investigators believe it is probable "that one important difference between the optimum type and the type who overcompensates and strains his circulation is that the former keeps brain and heart well supplied with blood but does not flood the rest of his body, while the latter has a marked increase of flow to all parts and so throws this unnecessary extra work upon the heart." No very convincing evidence has, however, been presented for this very attractive hypothesis. This condition of compensation with only slightly increased cardiac efforts continues in different cases for varying lengths of time. In the optimum class, loss of consciousness from anoxemia of the cortical cells develops before circulatory failure sets in. In the other types it develops earlier. The cause of the circulatory failure has been interpreted in different ways:

The fact that it is initiated by a fall of diastolic pressure, followed rapidly by a decline of systolic pressure, has been interpreted as indicating that the primary effect is due to a failure of the vasomotor mechanism (Whitney). This is soon followed, however, by a decreased discharge of the heart interpreted as an effect of anoxemia.

The more extensive investigations of Greene and Gilbert, both on man and animals, indicate however, that a different explanation may probably be given to this crisis. The salient features of the circulatory failure are described as follows: "In the crisis and during the post-crisis stages, blood-pressure undergoes greater and more rapid variations. The rule is that the pressure very gradually falls during the post-crisis and until the respirations cease. The heart slows down during this phase and the pulse amplitudes increase. Consequently, the diastolic pressure falls rapidly while the systolic pressure is maintained or may even rise. The maximal systolic pressure of this cycle is usually not reached until 20 to 40 seconds after respirations cease. The pressure events just described are followed by progressive and rapid decrease of both systolic and diastolic pressures with decrease in pulse rates until the pulse can no longer be distinguished, and the pressure remains constant at about 15 to 20 mm. Hg. The length of time required for the entire post-crisis cycle is from three to five or more minutes after respirations cease." (Greene and Gilbert.) Such experiments clearly indicate that the early fall of diastolic pressure is due to cardiac slowing rather than to a failure of the vasomotor mechanisms.

Further studies by the aid of the electrocardiogram have shown

that the first slowing of the post-crisis period is due to an accentuated vagus tonus and not to an effect of anoxemia on the heart. Through this vagal mechanism the rhythmicity of the *S–A* node is entirely abolished and the *A–V* node or some still lower rhythmic center becomes the pacemaker. If, however, at this stage the vagi nerves are cut, the normal rhythm again develops in the *S–A* node and the heart accelerates. Only in the last stages of anoxemia does the heart slow down, but in such events the *S–A* node remains the pacemaker to the last. These observations are important as showing the extreme resistance of the heart to very high grades of anoxemia. They also give a clue as to the possible cause of cardiac dilatation. This is apparently not due to a loss of cardiac tonus due to anoxemia nor to an increased venous pressure, but owes its existence entirely to the fact that the heart dilates to a greater extent in the longer diastolic pauses when it becomes slower in rate.

The Reaction of Diseased Hearts.—It is generally supposed that high altitudes are bad for "weak" or diseased hearts. At higher altitude levels such individuals notice unusual shortness of breath, palpitation, general exhaustion, and often decompensation or pulmonary edema develop (*Medical Research Manual*). This has, in a manner, been confirmed in studying the circulatory reaction in subjects with various cardiovascular disorders. As already indicated, some difference exists even in individuals with supposedly normal hearts, and it is apparently related to this instance to the physical fitness of the individuals. In the same subject, however, it varies from day to day, being modified even by minor infections, such as acute colds, etc. Subjects with irritable heart show evidence of a pending circulatory failure before normal hearts. Subjects with even moderate degrees of arteriosclerosis show an early cardiac acceleration and a marked rise of arterial pressures. Arrhythmias when present become exaggerated. Thus occasional extrasystoles may be supplanted by tachycardias of ectopic origin, and a tendency to block may be aggravated. The more serious cases, however, are associated with organic lesions. In valvular lesions the reaction depends largely upon the degree of compensation. Mitral stenosis is especially unfavorable; compensated mitral insufficiency cases react more favorably.

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CHAPTER XXI.

AFFECTIONS OF HEART MUSCLE ASSOCIATED WITH TOXEMIA, RETROGRADE CHANGES, INFILTRATIONS AND REPAIR.

When the nutrition of the heart cells is impaired or when they are submitted to chemical or infectious influences of a toxic nature, their metabolism is altered. The intracellular physico-chemical processes and perhaps the "molecular movements" are disturbed. Many chemical agents also increase or decrease the rate, amplitude and vigor of cardiac contractions. Thus, drugs like adrenalin and digitalis stimulate, and others, such as alcohol, chloroform, ether, chloretone, chloral and pituitary extract, depress the contractile function.

Still another class of substances, as the bacterial toxins or the split products of bacterial proteins (typhoid), act at once to stimulate the heat production and affect the rate, amplitude and vigor of contractions (Cleghorn). Since it is possible to cause such functional disturbance before histological changes have had time to develop, it may be assumed that when the heart is submitted to these influences in disease, disturbances of function generally precede parenchymatous changes, the latter occurring when the deleterious influences persist for a longer time. They are, therefore, *effects* rather than *causes* of disturbances in function (Aschoff).

The parenchymatous changes set up vary with the nature of the toxic influence, its period and intensity of action; but they are probably not fundamentally different in the various infections (Krehl). They consist in milder cases (*e. g.*, acute infections, typhoid) of granular degeneration, in more severe or prolonged cases of fatty, hyaline and calcareous degeneration (*e. g.*, after diphtheria) and in cases of circulatory disturbances of hydropic or fatty change. Toxic agents, and particularly those due to infections, are not restricted in their action to muscle cells alone, but either simultaneously or secondarily affect the vascular system, causing hyperemia with exudation of serum, lymphocytes and leukocytes. If the infectious organism (*e. g.*, pus cocci) themselves lodge in the heart, the attraction of polymorphonuclear leukocytes is great, and their extravascular massing may give rise to circumscribed abscesses or more diffuse suppuration. Such inflammatory infiltration may, by pressure or disturbance of parenchymatous tissue, be the *cause* of *added* functional disturbances.

If, as frequently happens, these infiltrations and abscesses form in regions such as the auriculoventricular septum or the papillary muscles, they may involve the conducting system of Tawara and so be the cause of serious or fatal derangements of the heart.

When the climax of retrograde changes has passed, repair sets in. This means the resorption of necrotic tissue by endothelial leukocytes, the proliferation of fibroblasts and the formation of new connective tissue. When, subsequently, the scar tissue contracts, it may either compress really vital regions of the heart or shut off the blood supply to certain regions. In either case it may be regarded as the cause of disturbances in function.

DISTURBANCES OF THE CORONARY CIRCULATION.

Disturbances of the coronary blood supply may be considered as of two kinds: (*a*) Those due to occlusion of vessels (thrombosis, embolism) and (*b*) those due to dynamic derangements of the circulation (coronary sclerosis).

Pathological Physiology of Coronary Occlusion.—Although the existence of an anastomosis between the branches of the right and left coronary systems has been anatomically established (Hirsch and Spalteholz, Merkel),[1] and a further communication exists by the Thebesian vessels with the ventricular cavities (Pratt), it is evident from animal experiments that when a main branch is suddenly occluded these collateral vessels are not sufficient to maintain the beat of the heart for a long period of time. Death often follows shortly after the ligation of the left coronary ramus, according to the experiments of Cohnheim and Porter. Nor do the recent experiments of Hirsch and Spalteholz, who kept animals alive for two weeks after ligation of the left coronary vessel, prove the functional sufficiency of this collateral circulation, for Miller and Matthews have subsequently shown that, if allowed to live, animals in which the left coronary had been ligated succumbed within twenty-six to ninety days with symptoms typical of cardiac insufficiency. On the other hand, such experiments clearly indicate that in the majority of hearts the collateral circulation is sufficient to maintain the beats for a considerable interval of time. This applies equally to the blood supply of the conducting system, for Kahn[2] has shown that ligation of the central branches supplying this system is no more serious than the involvement of other coronary branches. Death from ligation of the coronary vessels occurs only after days or weeks and is not due to primary cardiac anemia but to the fact that this

[1] For recent work on the anatomy and anastomosis of coronaries, *cf.* Crainicianu (Arch. f. path. Anat., 1922, **238**, 1).

[2] For details of blood supply of the conducting system, *cf.* Haas (Anatom. Hefte, 1911, **43**, 627), also Gross (The Blood Supply of the Heart, New York, 1921).

causes extensive degenerative changes. In ligating large superficial branches these changes involve chiefly the subendocardial layers, the epicardial layers being affected relatively less (Smith).

The signs following sudden occlusion depend upon the size and nature of the vessel involved. Occlusion of the main left coronary artery or its branches is often not followed by any immediate change except the production of an occasional ventricular extrasystole. These, however, gradually disappear and one week after ligation are very rare. The heart rate continues normal, but the drop of the maximal and rise of the minimal pressure within the ventricles, as well as the slower rate of systole, give evidence of an impaired cardiac contraction (Porter). Upon ligating the right coronary artery, which supplies the right auricle as well as ventricle, the preliminary extrasystoles of auricular as well as ventricular origin are followed by a tachycardia, which is rapid in its onset and may last from a few seconds to thirty-five minutes (Lewis).

These conditions of comparative regularity may persist only for a few moments or may extend over hours and days. Then follow signs that the heart is failing. The chambers dilate and ventricular systole becomes incomplete (Porter, Miller and Matthews). Without further signs of irregularity the rapidly beating ventricles suddenly go into fibrillation. The blood-pressure falls rapidly and death results from acute anemia of the respiratory and cerebral centers.

Electrocardiograms resulting after coronary ligation have been especially studied by Kahn and Smith. The chief aberration occurs in the *T* deflections, the *R* wave remaining relatively normal. In general, the amplitude of the *T* wave becomes greater, but on the second day it is replaced by a negative wave which persists from three to five days. This is interpreted as due to a prolonged negativity at the apex, Smith believing that it is especially marked when degenerative changes occur in this locality as a result of ligating the branches of the left descendens or circumflex rami. Kahn, however, appears to have obtained similar effects upon ligation of the septal branches alone.

Clinical Manifestations of Coronary Embolus and Thrombosis.—Closure of the large coronary vessels is known to occur more frequently from thrombosis than from the lodgment of an embolus. On postmortem, a characteristic anemic infarct is found. The symptoms vary considerably. Herrick recognizes four types of cases as regards symptoms:

(*a*) Cases of instantaneous death, a group described by Krehl, in which there is no death struggle, the heart and respiration stopping together.

(*b*) Cases of death within a few minutes or hours. These are cases that are found dead by the physician, who is hastily summoned, and in which death is, no doubt, due to ventricular fibrillation.

(*c*) Cases in which the patients are attacked by a painful angina of the classical type, which is, however, more enduring than ordinary angina, often lasting for hours. The heart is usually rapid (140 or more per minute), but may be slow (Krehl), and extrasystoles or partial block may occur. The pulse is weak, the blood-pressure low and the heart sounds feeble. Dyspnea and cyanosis are absent.

(*d*) Cases with similar but milder symptoms, *e. g.*, slight precordial pain in which the condition remains unsuspected. Such cases may live for years, as is shown by the fact that when they come to autopsy the entire obliteration of large vessels, like the descending ramus, is shown to have existed for years without symptoms (Birch-Hirschfeld).

The electrocardiograms in the latter group, so far reported, resemble those obtained in experimental animals, *i. e.*, are characterized by exceptionally large negative *T* waves. As these waves are apparently associated, however, with many myocardial affections, their presence may not be considered diagnostic of coronary obstruction. Their sudden appearance, however, in previously normal electrocardiograms may be of definite diagnostic value.

Dynamic Anemia of the Heart.—Pathological Physiology.—By *dynamic anemias* we will understand those forms of deficient blood supply which result from a dynamic change in the circulation, as distinguished from the *essential anemias* resulting from alterations in the composition of the blood.

The quantity of blood passing through the heart is determined by the height of aortic pressure and the total resistance in the coronaries (*i. e.*, vasomotor tonus, ventricular tonus and intraventricular pressure). In addition, however, the heart possesses a more direct mechanism of adapting its blood supply to its immediate needs. This is accomplished through the compression of the intramural vessels which acts to propel blood through the heart at a velocity which is directly proportional to the rate and amplitude of contraction. This is an exceedingly important mechanism, for it tends to compensate for changes otherwise tending to reduce the blood supply. This may be shown by passing adrenalin through a perfused heart. When the heart is perfused at a constant pressure with an oxygen-free solution it does not beat. Adrenalin then unfailingly causes a decreased flow due to a constriction of the peripheral coronary vessels. When the heart is perfused with an oxygenated Ringer's solution, on the other hand, and is beating, adrenalin increases the blood flow, since it simultaneously increases the rate and amplitude of ventricular contraction, which is sufficient to overpower the constriction effect upon the coronary vessels themselves. The writer has observed, furthermore, that an increased flow may still occur if, while the adrenalin action is at its maximum, the perfusion pressure is somewhat reduced. We have other evidence of the value of this direct mechanical regulating influence on the coronary circuit. When the

blood-pressure lowers after hemorrhage the heart may accelerate to such a degree that a larger coronary blood flow actually occurs in spite of the lower arterial pressure (Wiggers) (Fig. 140).

In view of the fact that the heart normally accelerates as the blood-pressure lowers, it is questionable whether a dynamic anemia sufficient to modify cardiac functions ever occurs from an alteration of the blood-pressure alone. After severe hemorrhages and in shock, the writer has never observed irregularities, nor were the functions of conductivity and contractility impaired in experimental animals.

This important protective mechanism depends for its existence upon the elasticity of the coronary vessels, and can operate only inadequately when they have become hardened by sclerosis or calcification or obliterated by endarteritis. Hence, when these conditions supervene the heart has suffered a great loss. If, now, the

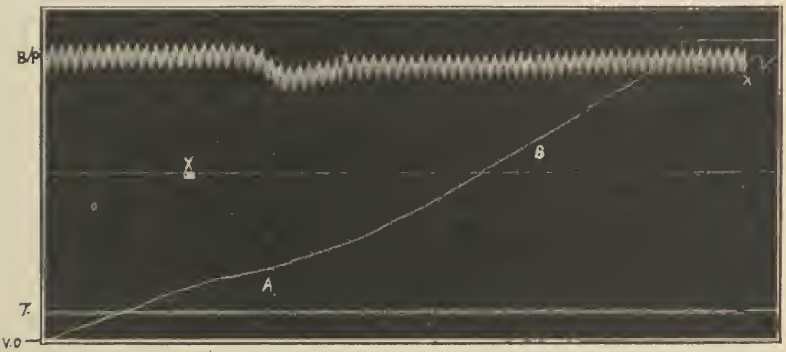

FIG. 140.—Effect of hemorrhage on coronary blood flow. *V.O.*, rate of flow; *B.P.*, carotid mean pressure; *A*, immediate reduction in flow at onset of hemorrhage; *B*, compensatory increase.

arterial pressure lowers or the heart increases in rate, the flow cannot be increased to the needs of the heart. If the arterial pressure rises and the work of the heart is increased, no appreciable increase in coronary flow can occur. It follows that a dynamic anemia only seriously affects the essential function of the heart when alterations in the vessels themselves occur.

Clinical Manifestations of Coronary Sclerosis.—Sclerosis of the coronary vessels follows many infections or toxic agents, but syphilis holds first rank as a causative factor. It is always associated with parenchymatous degeneration that can be only partly accounted for by the altered blood supply. These may themselves give symptoms of toxic myocarditis as later considered. But the best single symptom usually regarded so suggestive of coronary impairment is the occurrence of *angina pectoris*.

The symptom-complex designated as angina pectoris is composed

of three elements: The intense pain in the cardiac region sometimes radiating to the left arm, the sensation of ring-like thoracic constriction and the sensation of fear and of impending dissolution.

The relation of coronary sclerosis to angina is, however, by no means settled, as many cases come to autopsy who have never experienced anginal pains. Allbutt, in 1915, completely denied the sclerosis hypothesis (see below). It is perhaps true, as Mackenzie observes, that sclerosis without impairment of the heart is not sufficient to produce angina, at least the fact that many severe cases of sclerosis that come to autopsy show no signs of angina during life may be so explained. While sclerosis without angina may thus exist, it is very probable that all typical cases of angina are accompanied by some degree of coronary involvement.

The cause of these sensations has been the subject of frequent discussion. It is often assumed, in a very general fashion, that the pain is due to a process similar to that which takes place in skeletal muscles during fatigue or overstrain—that muscular pain is, in short, an evidence of overstrain. This is the statement of a fact rather than an explanation, however. More definitely, it has been suggested that an impaired blood supply is the cause of painful sensations. The intense pain resulting from shutting off the blood supply from a limb is cited as a common example. Furthermore, it has been found that the pain and the subsequent paresis which occur during exercise in the condition known as intermittent claudication (Charcot's) is associated with arteriosclerosis of the limb vessels (Erb). Hence, it has been assumed that, while the blood supply may be sufficient during rest, the increased demand during exercise cannot be supplied, hence the pain occurs. This explanation is not entirely sufficient to account for those anginoid attacks which frequently occur without exertion.

It has also been frequently assumed that a vasoconstriction of the coronaries occurs which further narrows the caliber of the vessels that are already reduced by sclerosis. The demonstration that the coronaries possess vasomotor nerves (Porter, Wiggers) forms a basis for such a theory, but it remains to be demonstrated that such a constriction is the cause of angina.

Admitting that pain is associated with muscular exhaustion, and that this may result from an inadequate blood supply, the exact mechanism through which pain sensations are generated remains difficult to explain. In regard to this, two general theories have have arisen: It may be due to the chemical stimulation of waste or fatigue products, or the mechanical pressure of a high degree of tonus on the sensory nerves which presumably leave the heart *via* the sympathetic and vagus (Müller, Goldschneider, Krehl) or *via* the depressor nerve (v. Cyon). Again, others hold that cardiac sensory nerves have not actually been demonstrated and that the heart,

in common with other internal organs, is not capable of recording pain. On the other hand, it may be able to so modify the irritability of the spinal segments from which its nerves arise that the pain is referred to the superficial sensory nerves having their terminals in the same segments. In this way the reflexes from the heart would involve the lower cervical and upper thoracic nerves and account for the viscero-sensory pain reflex in the chest and left arm during attacks of angina (Mackenzie). In a similar way a viscero-motor reflex may be set up, causing the muscles innervated from the same segment to contract. This view attributes the sense of constriction to the tonic contraction of the intercostal muscles.

Clifford Allbutt believes that the theory of myocardial vascular spasm is untenable and that angina is due to a stretching of the adventitia of the aorta (in which sensory Pacini's corpuscles have been demonstrated), or of the fibrous structures around the heart.[1]

Electrocardiographic studies of cases with angina pectoris have recently been made by Willius and Bonsfield. They find that while the *Q R S* complexes are low and broad and the *T* wave frequently inverted (indicating impaired impulse conduction through the myocardium), no changes were found that may be considered pathognomonic.

THE AFFECTIONS OF THE HEART DUE TO EXOGENOUS TOXIC INFLUENCES.

The chemical substances that affect the functions of the heart may be classified as exogenous and endogenous. A consideration of the exogenous agents belongs more properly to the province of pharmacology and toxicology. We shall, therefore, deal here, by way of illustration, merely with chronic alcoholic intoxications and the so-called "tobacco heart."

CHRONIC ALCOHOLIC HEART.

Pathological Physiology and Histology.—Whatever may be our opinions as to whether the "occasional" or therapeutic use of alcohol causes thorough reflexes or associated psychical stimulation, an improvement or an impairment of the cardiac functions, it is well established that its immoderate use always causes a depression of the heart, as in the case of intravenous injections in animals. In "heavy drinkers" we may assume that the heart is continually bathed in a weak alcoholic solution which tends to depress its activity and reduce its output. If continued for a long time this leads to loss of tonus and results in dilatation. It is this direct toxic influence on the heart muscle which is primarily responsible for its impaired action.

[1] For a discussion of these views, *cf.* Jour. Am. Med. Assn., 1918, **70**, 1030.

Another influence soon supervenes, however. Alcohol is a food and represents a high caloric equivalent, 1 gm. yielding 7 calories, as compared to 3.7 calories yielded by 1 gm. of sugar. The heart in connection with other organs must take part in its oxidation. If a proportionate number of calories of other food should be withheld, it is possible that the alcohol would be burned completely and in normal fashion. Usually, however, it is added to an already sufficient caloric intake, and then it acts to spare the fat which is stored in various regions. Among these are the connective tissue of the abdomen and that around the heart. This is probably the reason that the fatty heart is most frequently associated with the intake of malted liquors which contain, in addition to their alcohol, other substances of caloric value. Such fatty deposits may further diminish the capacity of the heart for effective work by mechanically interfering with its movements. These deposits occur not only around the heart, but penetrate with the connective tissue and cause an infiltration of the myocardium, or fat may also appear within the muscle cells. Virchow taught that this represented a conversion of the muscle protein into fat as a result of a toxic influence or a reduced blood supply, and, following his teaching, such fatty degeneration was to be carefully distinguished from fatty infiltration. According to Lusk, who gives another and a more probable explanation, there is no essential difference between infiltration and degeneration. A reduced local circulation (such as must naturally result during the weakened cardiac action under alcohol) may cause an imperfect local oxidation of the lactic acid normally found both within and without the cell. This incomplete oxidation of carbohydrate causes an attraction of a superfluously large quantity of fat to the sugar-hungry cell, which is deposited in and around the cell. According to this conception, the intracellular fatty degeneration is not the cause but the result of impaired function.

Clinical Manifestations.—The condition may manifest itself by various signs and symptoms which accompany cardiac dilatation and myocardial insufficiency (see page 566). Inability to indulge in customary muscular activity and pressure sensations in the chest are among the first subjective manifestations. These may be the only symptoms so long as the heart is able to maintain an effective circulation through the tissues. The medullary centers are the first to respond to any failure in this respect, by increased respiration, dyspnea and heart acceleration.

As dilatation increases, we may get symptoms on the part of the heart itself—extrasystoles and the presence of functional murmurs. The pulse is always feeble and the blood-pressure usually low. The cardiac area is enlarged, as indicated by percussion and by the orthodiagram. This enlargement may be merely the result of fatty infil-

tration and be accompanied by an actual atrophy of the muscle cells, or it may be accompanied by some hypertrophy, as in the Munich beer heart. The symptoms of hypertrophy are entirely obscured, however, by those of injured myocardial function, which may supervene and continue until all the symptoms characterizing heart failure are present (see page 566).

THE "TOBACCO" HEART.

While the question as to the effect of tobacco on the heart is an old one, the available accurate information is still scanty. This is due, in part, to the great variety of factors involved, and, in part, to the fact that the effects produced by injection of nicotine solutions in acute experiments may not duplicate the effects on individuals who have acquired a tolerance for tobacco. There is evidence that the use of tobacco causes acute changes in the caliber of blood-vessels and that blood-pressure increases after smoking (Lee, Bruce, Miller and Hooker), but the inference that this necessarily leads to arteriosclerotic changes, involving especially the coronary vessels, has not yet graduated from the status of an hypothesis.

More recent investigations have concerned themselves with changes induced in cardiac rate and rhythm. The chief action of nicotine is on the ganglion cells interposed in the vagus and sympathetic pathways. The sequence in which the ganglion cells are affected determines the resulting effect upon the heart rate. Consequently, the heart rate may be slowed, accelerated or unchanged. Such effects have also been noted experimentally. Thus, Pezzi and Clerc, Bull, Clerc and Pezzi observed an initial bradycardia after nicotine injection in dogs, followed by a tachycardia. Furthermore, by the use of the electrocardiograph they observed a variety of irregularities, such as premature systoles, incomplete heart-block, *A–V* rhythm and complete dissociation of auricles and ventricles. All of these effects they attributed to the simultaneous stimulation of vagus and accelerator ganglionic synapes. It is questionable, however, whether many of these effects may not be due to direct action on the heart muscle.[1]

Clinical Manifestations.—The chief cardiac manifestation of chronic nicotine intoxication consists of rapid heart action, cardiac irregularities, premature systoles usually predominating when, for any reason, the heart slows. Neuhof has recently reported 2 cases of sino-auricular block in tobacco users which disappeared on discontinuance of the use of tobacco. The size of the heart remains unaffected. The blood-pressure is said to be higher than in normal individuals, although no careful statistical compilations as regards this question appear to have been made.

[1] For articles dealing with the possible deleterious effects of carbon monoxide in tobacco smoke, *cf.* Baumberger (Jour. Pharm. and Exp. Therap., 1923, **21**, 23).

THE AFFECTIONS OF THE HEART DUE TO ENDOGENOUS TOXIC INFLUENCES—GOITER—ANAPHYLAXIS.

Among endogenous substances may be classed all the split products of digestion and metabolism. There is little positive evidence that such as probably enter the circulation, *e. g.*, amino-acids, urea, uric acid and xanthin derivatives, creatinine, etc., exert any recognized influence on the functions of the heart or that they are capable of producing histological changes. Of greater significance are the changes in the cardiac functions which accompany disturbances of the ductless glands, notably the thyroid.

THE THYROID HEART.

Clinical Physiology.—Baumann, in 1896, isolated a non-protein, iodine-containing body from the thyroid gland, which he termed *iodothyrin*. When this substance, or an extract of the thyroid gland, is injected into experimental animals, it causes an increased or decreased heart rate and a fall of blood-pressure.[1]

More recently, Kendall has succeeded in isolating a crystalline body of known composition and called it *thyroxin*, which if given with amino-acid has similar effects on metabolism and probably also on the circulation.

The cardiac acceleration is apparently due partly to a stimulation of the accelerator mechanism and partly to a direct action on the cardiac muscle, the inhibitory mechanism being apparently unaffected (Cushny). The fall of blood-pressure is due to a peripheral dilatation of the bloodvessels which is, according to v. Cyon, a reflex caused by the stimulation of the depressor endings. Since similar effects have been produced both in animals and man by feeding large doses, and since these, in turn, correspond in a certain manner with the symptoms noticeable in patients suffering from exophthalmic goiter (Graves's disease), it is generally inferred that in this disease the internal secretion is poured into the blood in abnormal amounts, which give rise to the clinical conditions associated with the affection (v. Fürth). Further corroboration has recently been added by Sanford and Blackford, who showed that a similar effect occurs in animals when the serum of goiter patients is injected into them. The first injection produces tolerance for subsequent ones. The effect is not abolished by atropine, and in this way it differs from the depression of blood-pressure produced by other tissue extracts.

Clinical Manifestations.—The chief cardiac symptom associated with exophthalmic goiter consists in the persistent or easily provoked

[1] For a review of the literature and additional evidence that the depressor effect bears no relation to the iodine content of the extract injected, see Fawcett, Rogers, Rahe and Beebe, Am. Jour. Physiol., 1915, **36**, 113.

tachycardia accompanied by palpitation. The tachycardia, which usually does not disappear on resting, is of the sinus variety, although attacks simulating paroxysmal tachycardia have been reported. It is supposed that this is due to stimulation of the accelerator nerves, which are rendered hyperactive. The fact that epinephrin causes a greater acceleration in thyroid cases is in favor of this hypothesis (Goetsch).

The cardiac area in the early stages is normal, but later the heart may become enlarged. Accidental murmurs are often present. The apex beat is vigorous and sometimes out of proportion to the amplitude of the arterial pulse. In many cases, however, the pulsations in all arteries are particularly vigorous and a capillary pulse is often observed. Indeed, all the tissues of the body may be pulsating. Irregularities are often present, especially in advanced cases. These consist of extrasystoles and auricular fibrillation (White and Aub). The blood-pressure is apparently variable, but a hypotension is less frequent than a hypertension (Plummer, Taussig). There is no doubt that other pathological processes play an important rôle when the pressure is elevated and the pulse pressure increased (Kraus and Friedenthal). In addition to the characteristic complexes due to the irregularities mentioned above, the electrocardiogram shows a constant increase in the amplitude of the *T* wave (White and Aub). Left ventricular preponderance is only occasionally seen.

THE ANAPHYLACTIC HEART.

If a guinea-pig be sensitized by the peritoneal introduction of a small quantity of foreign serum and ten days later a second dose of about 5 mg. be given, the animal becomes uneasy, dyspneic, paralyzed and dies with lightning rapidity. In the case of the rabbit and dog the symptoms are less severe and recovery often follows. The symptoms are spoken of as the *anaphylactic reaction,* or when more severe, as *anaphylactic shock,* and are of interest in relation to the *serum reaction* in man.

The cause of the serious symptoms and rapid death have been variously interpreted as follows: (1) A paralysis of the vasomotor center (Richet); (2) a paralysis of the peripheral vasomotor mechanism (Edmunds); (3) a paralysis of the respiratory center (Rosenau and Anderson, Gay and Southard); (4) a spasm of the bronchial muscles causing asphyxia (Auer); (5) a general spasm of non-striated muscle (Anderson and Schultz); (6) capillary dilatation due to the toxic action of histamine on endothelial cells (Dale and Richards).

The immediate cause of death apparently varies in different animals and depends upon where smooth muscles are especially developed. Thus, in the guinea-pig, in which the bronchial system is highly developed, death is due to a rapid constriction of the bronchial

muscles leading to asphyxiation. In the rabbit the chief effect seems to be on the heart. Injections of foreign proteins into previously sensitized rabbits cause a rapid rise of blood-pressure, which is maintained at a high level for some time and then falls. Coincidently, the heart slows, due to a partial block (*e. g.*, a 3 to 1 rhythm), whether the vagi are intact or cut (Lewis and Auer). This reaction occurs very promptly after injection (thirty seconds to three minutes) (Robinson and Auer). It is as yet uncertain whether this is due to a spasm of the coronary arteries or not. Direct evidence has, however, been submitted that a spasm of the pulmonary artery takes place, and which is, in part at least, responsible for the damming back of blood induced in the right ventricle (Coca). In dogs, the anaphylactic reaction expresses itself chiefly by a rapid fall of blood-pressure, lasting about three and a half minutes (Biedl and Kraus). The action resembles that produced by the injection of Witte's peptone and also that of the toxic portion of Vaughan's split proteins (Edmunds). Furthermore, Dale and Laidlow have shown that a similar effect is produced by the injection of histamine, and are inclined to believe that in anaphylactic shock, histamine or histamine-like substances are formed from the amino-acid, histidine, which is present in all complete proteins. Experiments indicate that the chief cause of the fall of blood-pressure is due to accumulation of blood in the liver (Edmunds, Manwaring). This accumulation has been explained as due to: (*a*) A dilatation of the smaller tributaries of the portal system (Edmunds) and (*b*) to a constriction of the hepatic veins, which are apparently supplied with a greater abundance of muscle fibers in the dog than they are in any other animal (Simonds). There is considerable evidence, however, which indicates that the peripheral effects in anaphylactic reactions are not entirely limited to the liver. The trend of recent work (Dale and Richards) indicates that the vascular changes, especially in the abdominal vessels, are quite comparable to those produced in toxemic shock, in which the formation of histamine or histamine-like bodies is also a factor (*cf.* page 602).[1]

While the changes in the peripheral bloodvessels undoubtedly account for the predominant effects observed in the circulation, the heart does not entirely escape in dogs. Myocardiograms indicate that there is a slight weakening of the heart beat (Pearce and Eisenbrey, Edmunds). Electrocardiographic studies (Robinson and Auer) indicate that in this animal partial or complete block fails to occur in about one-half of the cases. The heart is slower and the ventricular complexes change. The *S* depression is deeper and the *T* wave exaggerated. The cardiac disturbances are not the result of low blood-pressure, nor does central inhibition play a part.

[1] For brief and clear discussions of the physiological significance of anaphylaxis, see Dale (Proc. Roy. Soc. London, 1920, **91**, 126) and Wells (Physiol. Rev., 1921. **1**, 62).

MYOCARDITIS IN ACUTE INFECTIONS.

Myocarditis may accompany or follow diphtheria, scarlet fever, influenza, pneumonia, syphilis, infections with the staphylococcus, streptococcus and gonococcus, and less frequently typhoid fever. The cause and effect relations of parenchymatous and interstitial changes and the altered function have already been indicated. In toxemic or infectious diseases the efficiency of the heart and circulation may suffer, not only on account of the myocarditis, but also because of the associated elevation of temperature and changes in the ventricular blood supply.

The idea that changes in the peripheral circulation can secondarily involve the heart has been widely accepted in recent years. There is distinct evidence that cardiac power itself is not exhausted in death from infectious fevers for: (*a*) Hearts of animals and of man have been revived after death, and (*b*) circulatory failure has often been warded off by the use of adrenalin or abdominal compression. (For literature, see MacCallum.) It cannot be doubted, therefore, that the decrease in cardiac efficiency and even its final cessation is aided by the failure of the peripheral circulation. The demonstration that the heart is not alone concerned has been regarded by some as proof that the vasomotor center necessarily fails. This idea was given impetus by a series of researches published by Romberg and his pupils (1896–1899), in which it was attempted to show that during the course of such illnesses, as diphtheria, pyocyaneus and pneumococcus infections, the cause of circulatory failure was a paralysis of the vasomotor center. This view has received apparent support from the investigations of Rolly and, more recently, from those of Yabe, in the case of diphtheria toxin. The thorough experiments of Porter and his pupils, however, indicate definitely that both in diphtheria and pneumonia the vasomotor center is normal to the end.

DIPHTHERITIC MYOCARDITIS.

Pathology.—The many deaths resulting from diphtheria are due largely to its detrimental effect on the heart, which is seriously affected in 10 to 20 per cent of all cases (Romberg, Schwartz, Smith). Circulatory involvement may occur during the course of infection (usually the first or second week) or during convalescence.

It has been found that by the second week the cardiac changes are largely parenchymatous in character, though interstitial exudates occur. (See Röhmer, McCulloch, Tanaka (literature.)) These may or may not involve the conducting system of Tawara (Tanaka, Röhmer, Leede). This can be gleaned from the following table, which is a partial list of the published postmortem reports:

PATHOLOGICAL CHANGES IN THE HEART AFTER DIPHTHERIA.

	Cases.	Myocardium.	Conducting system.
Mönckeberg . . .	1	Uniform fatty degeneration of all.	
Amenomeya . . .	12	Fatty and vacuolar degeneration of all.	
Heilhecker	6	Fatty degeneration.	No change.
Löw	3	Fatty degeneration.	Interstitial infiltration; fatty change.
Burger	12	Degeneration in all.	
Tanaka	15	Fatty degeneration in all (except 1 case).	
Leede	3671	Fatty hyaline degeneration	Bundle affected in part of cases.
Price and Mackenzie .	1	Cellular infiltration; fatty degeneration.	No change in bundle.

Clinical Interpretation of the Cardiac Conditions.—The intensity of the cardiac changes during the early and active period of infection is largely due to the poisonous effect of the diphtheria toxin, and is, no doubt, proportional to the quantity actually absorbed or unneutralized by antitoxins. In the majority of treated cases the heart shows only a tachycardia of sinus origin (Lutembacher). The rate may be as high as 135 to 172 per minute. In untreated cases the intensity of the toxic action is unequalled by that of any other infectious disease. According to Leede, death occurs in 54.16 per cent of cases during the first week, and of these 3.7 per cent die within the first twenty-four hours. There is little experimental evidence to support the view at one time in the ascendancy that death is due to peripheral vascular causes; on the contrary, death is apparently due to myocardial failure, of which various forms of irregularity occurring during the course of the disease are but expressions. In a large percentage of cases the heart is slow and irregular.

Studies of these have shown that they are caused by partial or complete block (Fleming and Kennedy, Price and Mackenzie, Hume, etc.), and electrocardiographic studies indicate that in such blocks left- and right-sided ventricular complexes are evident (Röhmer). Other forms of irregularities, such as nodal rhythm, premature auricular systoles, auricular flutter and paroxysmal tachycardia have been described. The arrhythmia often changes in type from day to day (Hume). These are undoubtedly brought on by destructions of various parts of the conducting system. Thus, Hume found a granular degeneration of the sinus node and an unaffected *A–V* node in a case in which nodal rhythm developed on the eighth to tenth day. A number of cases of block have been reported, however, in which no disturbances of the conducting system could be found (*cf.* Price and Mackenzie). In many instances it is impossible to say whether nodal rhythm is due to an increased irritability of the *A–V* node or to a depression of the sinus node (Hume, Clegg). Death from cardiac

failure is usually due to involvement of the conducting system, the development of the heart-block being especially serious (Smith, S. C., Allen). Sometimes the only changes found electrocardiographically before death are variations in the ventricular complexes, suggesting conduction disturbances in the bundle branches or their arborization. Thus, the *Q R S* complex is wider and of low amplitude, while the *T* wave is inverted (Röhmer). Right-sided dilatation always precedes death. Cardiac irregularities may not develop until convalescence has set in and the danger from cardiac failure is by no means over at this time (McCulloch). On the contrary, death may still occur suddenly and unexpectedly. Either tachycardia or bradycardia may be present. The changes evident in the heart are either tachycardia or bradycardia. The tachycardia is usually of the sinus variety, but cases of true paroxysmal tachycardia have been reported (Krehl, Hume). Sino-auricular block is frequently present (S. C. Smith). The heart, however, more often shows irregularities or a slow rate because of partial or complete heart-block. Especially interesting is the absence of auricular fibrillation (S. C. Smith), only a single reported case having come to my attention (Parkinson).

Evidences of dilatation are given by the increase in dulness, by the onset of functional mitral murmurs and by orthodiagrams. Dietlen has shown by the use of the orthodiagraph that the dilatation may increase progressively. The arterial pressure falls and the pulse is small. Venous stasis and edema often appear. Evidence seems to assure us that death in such cases is entirely traceable to direct cardiac failure.

In the stage of convalescence, death has been reported as occurring suddenly and without premonitory symptoms. It is probable, however, as Krehl remarks, "that death will occur unannounced less and less often as the physician examines the heart more and more extensively." By the employment of recent methods it is possible to detect early changes in conductivity which presage more extensive disturbances, and should warn against the employment of remedies tending to augment such a block (*e. g.*, digitalis).

THE HEART IN ACUTE RHEUMATIC FEVER.

With the general recognition that acute rheumatic fever so frequently excites an endocarditis, the fact that it causes a myocarditis, which may seriously affect the cardiac function, has been distinctly underemphasized. This is due, in part, to the fact that it has not been understood that signs regarded as characteristic of endocarditis (*e. g.*, systolic murmurs) may be produced by myocardial dilatation as well. The absence of pathological changes in the heart muscle during the early stages has also favored this view. More recently there has been a tendency to return to the older conception, viz.,

that a *carditis* is produced in which the involvement of the endocardium and myocardium cannot be differentiated by the symptoms.

The signs of acute myocardial lesions may occur early in the course of the infection, and are then brought about by the toxic influences on the heart; or they may occur late in the disease, in which case they are accompanied by degenerative changes in the heart cells by leukocyte infiltration or small cellular foci (Aschoff), which present a very typical appearance. They are composed of large atypical round or oval cells, which are frequently multinuclear and arranged around smaller bloodvessels and capillaries. These cells, in turn, are surrounded by a zone composed of leukocytes and plasma cells (Aschoff, Whitman and Eastlake).

Clinical Recognition.—Myocardial involvement may not always be easy to diagnose. Three signs are usually considered diagnostic, viz., dilatation of the heart, presence of systolic murmurs and changes in the rate and rhythm of the pulse. The heart rate is usually very rapid; the heart sounds are sharp and clear, often reduplicated or complicated by a soft systolic murmur. Dilatation is rarely severe enough to cause discomfort, breathlessness or edema (Poynton).

The occurrence of a soft, blowing systolic murmur may be without significance. More definite evidence of myocardial trouble is given when the heart becomes irregular (Parkinson, Gosse and Gunson). Extrasystoles occur early in the disease and probably indicate that the toxic action has produced a hyperirritable condition of the cardiac muscle. The writer has known them to occur two days after the onset of acute rheumatic fever. Auricular fibrillation and flutter have also been reported (Parkinson, Gosse and Gunson). Changes in conductivity appear somewhat later and undoubtedly accompany parenchymatous or interstitial changes in the heart muscle. Heart-block of various degrees present themselves, both sino-auricular and sino-ventricular block being met with. The heart is peculiarly susceptible to drugs producing heart-block (Mackenzie, Parkinson and others). It should be borne in mind, however, that during such infections the possibility should be remembered that the changes may be the result of medication rather than of myocardial lesions (*cf.* Sicard and Meara).

Outcome.—The acute myocarditis occurring early during a febrile attack, rarely results fatally, but the patient only occasionally makes a complete recovery. Poynton regards it as the threshold of organic disease. Most frequently, a chronic myocarditis supervenes which grows progressively worse as the years pass. The cellular exudates are absorbed, necrotic tissue disappears and fibrous tissue forms; but not infrequently the muscle cells continue to show parenchymatous degeneration and a degree of hypertrophy depending upon the concomitant valvular defects. Indeed, it is difficult after a number of years to separate the myocardial involvement directly due to the

previous infection and that due to impaired function arising from valvular lesions. The irregularities present during a chronic myocarditis may be caused by: (*a*) Sclerotic and fibrous changes, involving the conducting system and so producing a form of heart-block; (*b*) increased pressure in the auricles, producing extrasystoles and perhaps leading to auricular flutter or fibrillation; (*c*) areas of fibrous and muscular degeneration, involving the sinus region and auricle and causing auricular fibrillation. Dilatation readily occurs in such cases. This manifests itself in symptoms of dyspnea, venous engorgement and edema. The presence of a systolic type of venous pulse due to tricuspid insufficiency, a low arterial pressure and small irregular pulse are also characteristic. The cardiac area itself is enlarged.

MYOCARDITIS ASSOCIATED WITH SEPTIC INFECTIONS. EXANTHEMATOUS DISEASES, ETC.

The myocardial changes characteristic of the acute stages of rheumatic fever may also be present during septic infections of the myocardium with staphylococci, streptococci and gonococci, and, as a result of the unknown infection of scarlet fever (Rosenbaum) and occasionally after measles. In the virulent septicemias the accumulation of leukocytes and necrosis are greater than in acute rheumatic fever, and often result in abscesses of varying size. The same clinical cardiac symptoms which occur in rheumatic fever are present in varying degree. Dilatation, tachycardia, mitral murmurs and irregularities are typical. Because the myocardium is so severely attacked and because of the associated endocarditis the danger of heart failure during the acute attack is far greater in the septicemias than in rheumatic fever, but after recovery has occurred there is less danger of a subsequent chronic myocarditis.

Finally, mention must be made of the observations that a large variety of disturbances in rhythm, conduction and contractility may occur from the localization within the heart of the Trypanosoma cruzi (Chagas and Villela).

THE MYOCARDIAL CONDITION IN TYPHOID.

A study of the pathological and clinical signs during typhoid shows that the myocardium is involved at the height of the affection. In the early stages (first week) such pronounced changes in the circulation occur that they are often diagnostic. The pulse rate accelerates, but not in proportion to the fever. It usually reaches the neighborhood of 100. Its amplitude is large, the descending limb falls rapidly and is followed by a deep and prominent dicrotic notch, which is usually evident to the palpating finger. The systolic blood-pressure is generally lower, but the writer has found no reliable study

showing that the diastolic pressure is low during the first week. The pulse pressure is great, as one should expect. A capillary pulse may be present. During the existence of these signs no pathological

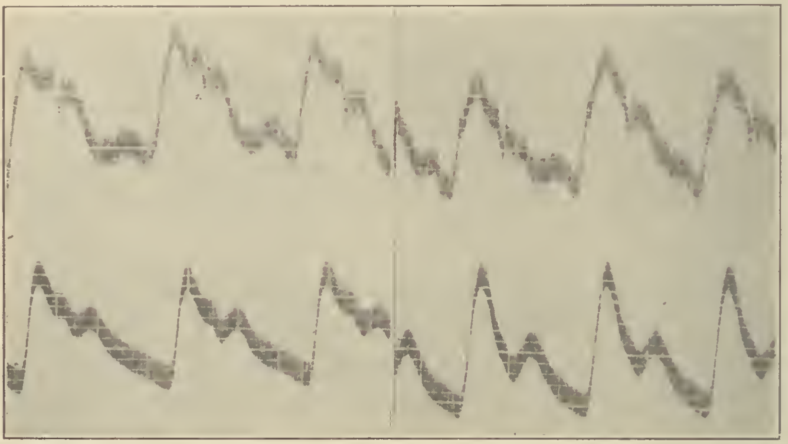

FIG. 141.—Simultaneous tracings of subclavian (upper) and radial (lower) pulses. (*a*) before and (*b*) after amyl nitrite.

changes are present in the heart. The entire circulatory complex is, therefore, referable to a peripheral change—apparently a *vasodilatation*. Further work, however, is required *to establish* this fact.

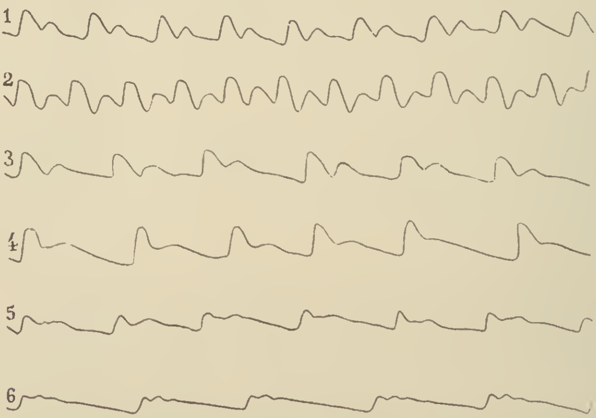

FIG. 142.—Series of sphygmograms taken on successive days in typhoid fever by Marey's sphygmograph. (After Marey.)

The writer has often pointed out to students that every form of cardiac and pulse change observed during the first week or ten days of typhoid infection can be well illustrated within a few minutes after

inhalation of amyl nitrite (Fig. 141). The systolic blood-pressure falls, the pulse pressure is increased, the pulse amplitude becomes larger, and the pulse more collapsing and dicrotic. As a result of a reflex through the vagus the heart accelerates and thus causes an abbreviation in the length of the pulse wave. If the heart beats too rapidly the dicrotic wave of one oscillation may be mounted on the upstroke of the next ascending pulse, *giving a superdicrotic effect* (Fig. 142, 2).

After the first week or two, the character of the pulse changes gradually until it often becomes more rapid, while its dicrotism disappears and its amplitude decreases. Its shape still indicates that the blood-pressure is low, a fact confirmed by the sphygmomanometer. The occurrence of granular degeneration, together with the fact that systolic murmurs, feebler first sounds or even a gallop rhythm occur, indicates that the myocardium is weakened during this stage.

The pulse rate gradually diminishes with the disappearance of the fever. Extrasystoles may be present, but disorders of conduction are rare (Pezzi and Selingarde). Cases have been reported, however, in which partial or complete block supervened and accounted for the slow rhythm. In these the well-known fatty changes and hyaline degeneration of the muscle cells, occurring late in typhoid infections, probably involved the His-Tawara system of conducting fibers.

THE HEART IN PNEUMONIA.

In uncomplicated cases of lobar pneumonia the changes in the heart and circulation are no greater than in any febrile process. The pulse at first is rapid and of large amplitude, the heart sounds are loud and clear and the blood-pressures are not far from normal (Newburgh and Minot). As consolidation progresses, dilatation of the right heart is often suspected and the arterial pulse may then become smaller and less forcible. Premature auricular or ventricular systoles often occur, but have not been demonstrated to be of any pathological significance (Cole).

When the case progresses to a fatal issue, death is usually due to respiratory failure and not to a failure of the circulation (Newburgh, Means and Porter, Newburgh and Porter). There are three periods of the disease in which serious failure of the circulation may appear. Before the crisis has been reached the pulse may become small and extremely rapid, sometimes reaching 140 per minute. The blood-pressure may be low and irregularities may appear (Mackenzie). The heart becomes dilated, the first tone impure and venous stasis may be present. From this condition the patient may either recover or succumb, with symptoms of collapse within twelve to thirty-six hours.

Very similar symptoms may occur at two other stages of the disease,

namely, during or after the crisis (Zadek) and during convalescence. At these times, however, they seem to be rarely fatal.

Three causes have been suggested for these circulatory crises, viz.: (*a*) A toxic paralysis of the vasomotor center; (*b*) toxic degeneration in the myocardium; (*c*) right-sided overwork, due to an increased resistance of the pulmonary circuit. Newburgh and Porter have shown experimentally that the first two factors are probably not concerned, and clinical evidence points to the fact that an increased pulmonary resistance is only a contributing factor. No doubt many of the serious attacks suddenly arising during the course of this infection may be attributed to the dynamic effects produced by transient disturbances in cardiac rhythm. Thus, Cohn reports fibrillation in approximately 10 per cent of cases examined, and some form of block in 30 per cent of a smaller series. There is little doubt that, owing to the increased pulmonary resistance, the anoxemia and the pyrexia, the right heart in particular is laboring under a greater strain. As long as the heart remains regular, however, it is able to compensate and maintain an adequate supply of blood to the left heart and in this way keeps up an efficient circulation. Under these conditions, it requires only the supervention of an irregularity as auricular fibrillation or a pronounced ventricular slowing, as in *A–V* block, to cause a prompt decompensation. Fortunately, such events are frequently transient and the heart is again allowed to compensate. If it persists, death follows. Finally, the possibility that circulatory embarrassment may result from oligemia must be borne in mind.[1] The blood is often concentrated (Sandelowsky).

THE HEART IN INFLUENZA.

There is still some difference of opinion as to the extent to which the influenza toxin affects the heart muscle. The bulk of pathological evidence (*cf.* Reports of British Research Committee, F. M. Smith, Symmers) as well as clinical observations (Mackenzie) indicate that, in uncomplicated cases, the heart reacts as in any febrile affection. The heart rate is increased and systolic murmurs may appear. Other observers (Eichhorst, Cumston, Hamburger, Minet and Legrand) believe that the cardial complications have been greatly minimized and an attempt has been made to designate one variety as *cardiac influenza*.

In the bronchopneumonic type, so prevalent in the second and third waves of the last epidemic, severe cardiac and circulatory failure was frequently observed. This appeared unexpectedly either some days after the onset of the disease or during convalescence, when all danger was supposed to have passed. The circulatory crises described apparently fall into three classes: In the first class, the pulse suddenly becomes more rapid (120 to 140) and decreases

[1] *Cf.* page 580.

in volume, the heart sounds become soft or muffled and occasionally systolic murmurs appear. Some evidence of dilatation may be found. Most impressive, however, is the patient's change of color, the cyanosis already present changing to a peculiar and characteristic dusky heliotrope shade. Undoubtedly, acute failure is suggested. Whether this is due, however, to the effect of the influenzal toxin itself or whether it may be attributed to a terminal effect of the marked anoxemia which is present, must remain undecided. A second type of circulatory embarrassment (found most frequently during convalescence but occasionally also during the course of infection) consists of sudden syncope, pallor, dyspnea and a very slow pulse. The probability is that heart-block, or a pronounced sinus bradycardia, is the causative factor in such cases. Finally, a condition of acute circulatory failure may occur with all the symptoms of toxemic shock (*cf.* page 583). As a marked capillary dilatation and injection, not only of the skin and mucous membranes but throughout the viscera, has been found (Symmers, *British Research Committee Report*), as well as a concentration of the blood corpuscles (Underhill and Ringer), the possibility that a true toxemic shock may occur must be kept in mind.

Considerable attention has been given to the post-influenzal changes in the heart. Two extremely different conditions may be present, viz., either tachycardia (100 to 120) or extreme bradycardia with a pulse rate usually from 40 to 50. A tachycardia is frequently accompanied by breathlessness on exertion, dizziness or weakness. According to Mackenzie, this may be regarded as an after-effect accompanying the general weakness which persists after an attack (Mackenzie, F. M. Smith), for no evidence of myocardial involvement is demonstrable. The bradycardias are not always of the same type. Cases have been reported in which the pulse rate fell as low as 15 to 19 per minute (Minet and Legrand). Most frequently bradycardias are of the sinus variety (de Meyer, Cockayne), but that varying degrees of heart-block may occasionally be responsible for such post-influenzal slowing is indicated by the fact that in 55 cases of slow heart rates reported by Cockayne, 19 were found to be due to partial *A–V* block and one exhibited evidence of a sino-auricular block. Apparently, the influenza toxin has a predilection for the *S–A* node, the auricular tissue and the conducting system (Hamburger).

THE HEART IN SYPHILIS.

Until recently it was supposed that when the Treponema pallidum invades the heart, it causes only slight parenchymatous changes, the cells undergoing no serious retrograde changes or necrosis. According to Warthin, however, both parenchymatous and interstitial

changes occur early. The former end in fatty degeneration, simple atrophy and necrosis; the latter lead to edema, interstitial infiltrations with leukocytes and lymphocytes and arterial impairment. When the blood supply becomes decreased as a result of endarteritis and sclerosis the proliferation of fibroblasts causes the formation of gummata. A favorite location seems to be in the septum between the auricles and ventricles, where they encroach upon the narrow His bundle and so interfere seriously with the heart's action. The left ventricle is apparently affected more often than the right. So it comes about that although the active phases of syphilis are rarely associated with cardiovascular disturbances a serious myocardial involvement often occurs many years after the acute disease has passed off (six to ten years) (Krehl).

The delayed effect of the syphilitic infection manifests itself in three directions: (*a*) The production of sclerosis and gummata interfering with special cardiac functions, as contractility or conductivity; (*b*) the presence of arteriosclerosis with its attendant symptoms; (*c*) the presence of aortitis, aneurysms and valvular lesions with their effects. All that has been said in other sections in regard to the signs and symptoms due to factors *b* and *c* applies to the syphilitic involvement of the heart, which cannot be separated from pure myocardial involvement.

To avoid repetition, we may limit ourselves to the evidences of direct myocardial change. Varying degrees of sino-ventricular block, as also complete block with the attendant Stokes-Adams complex, are frequent accompaniments of this disease. Auricular fibrillation is also a common result when the sclerosis involves the auricular musculature.

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CHAPTER XXII.

THE DIAGNOSIS AND SIGNIFICANCE OF ABNORMAL CARDIAC RHYTHMS.

Disturbances of cardiac rhythm arise when the functions of impulse origination (rhythmicity), impulse conduction (conductivity) or contractility are in some way affected. It is not possible, however, to base a practical classification upon the nature of the disturbance alone, as was at one time hoped, for the simple reason that most forms of irregularity result from the involvement of many functions. For this reason, the classifications were at first empirical and then, as our knowledge concerning their causes and relationships grew, they were necessarily varied to conform to scientific and practical standards alike. For the same reason, it may confidently be expected that they will continue to change, not only as to their groupings, but to a certain extent, also, in their nomenclature. We may venture the following classification:

CLASSIFICATION.

Disturbances of Impulse Initiation.

A. Homogenetic rhythms.

- I. Abnormal sinus rhythms (nomotopic rhythms).
  - (*a*) Sinus tachycardia.
  - (*b*) Sinus bradycardia.
  - (*c*) Phasic sinus arrhythmia.
- II. Ectopic rhythms.
  - (*a*) *A–V* rhythms (junctional or "nodal" rhythms).
  - (*b*) Idioventricular rhythms.

B. Heterogenetic rhythms.

- III. Premature systoles.
  - (*a*) Auricular origin.
  - (*b*) Atrioventricular origin.
  - (*c*) Ventricular origin.
- IV. Paroxysmal tachycardia of:
  - (*a*) Auricular origin.
  - (*b*) *A–V* nodal origin.
  - (*c*) Ventricular origin.
- V. Auricular flutter and fibrillation.
- VI. Ventricular fibrillation.

DISTURBANCES OF IMPULSE CONDUCTION.

VII. Heart-block.
   (*a*) Sino-auricular block.
   (*b*) Auriculo-ventricular block.
   (*c*) Bundle-branch block.
   (*d*) Arborization block.

VIII. Alternation of the heart beat.

DISTURBANCES OF IMPULSE INITIATION.

I. ABNORMAL SINUS RHYTHMS.

Clinical Physiology.—The *sinus region* of the heart is that posterior portion of the auricle which is bounded above by the superior vena cava and below by the coronary sinus, and which extends to the intra-auricular septum. It contains a set of peculiar muscle fibers and some nerve cells and fibers, collectively forming a club-shaped enlargement spoken of as the *S–A* node (Keith and Flack).

According to the most recent evidence, it is within this node that the heart beat is rhythmically inaugurated,[1] and hence it has been designated the *pace-maker* of the heart (Lewis). In the sinus region terminate the vagus and sympathetic fibers which normally exert their influence not only to modify the rate at which impulses are originated, but also to determine what part of the *S–A* node shall send them forth[2] (Zahn, Meek and Eyster).

The degree of vagus influence, which is estimated from the acceleration resulting when the vagi nerves are cut or their terminals are paralyzed by atropine, varies in different animals. Thus, in the cat, vagus section or the action of atropine produces an acceleration, while in the rabbit the rate is unchanged. In the dog, the vagus often exerts a rhythmic rather than a constant tonic action, so that the beats occur more rapidly during inspiration than during expiration, in fact, the heart may stop entirely during the latter respiratory phase. This rhythmic variation is abolished by vagus section, which proves that it is due to a central vagus influence (Fredericq).

The degree to which the vagus influences the tempo with which impulses are initiated in the sinus region of man likewise varies. The tonic vagus activity constantly increases, which accounts for the progressive slowing of the heart from infancy until adult life. Indeed, the figures of the average heart rate at different ages may be taken as an approximate index of the development of vagus control of the heart. The following figures have been compiled by Vierordt as average figures: At birth, 130 to 146; two years, 111 to 124; four years, 110 to 111; six years, 99 to 102; eight years, 97 to 98; ten years, 88 to 93; twelve years, 81 to 91; fifteen years, 81 to 87.

[1] *Cf.* page 27. [2] *Cf.* page 51.

During the period of adolescence and before the full power of the vagus over the heart becomes established, its tonus is apt to be periodic and the cardiac rhythm, therefore, not quite regular (Mackenzie, Friberger). This condition is manifested most frequently during rest and sleep, and disappears when vagus tonus is diminished, as in exercise. A rhythmic variation of vagus tonus, though not perceptible as producing pulse irregularities, is, nevertheless, present in the majority of adults. Usually, it is associated with inspiration and expiration, indicating that, as the respiratory center discharges during the phase of inspiration, it sends inhibitory impulses also to the vagus center, causing a cardiac acceleration. These periodic variations in rhythm may, however, occur without relation to respiration, indicating either that the cardio-inhibitory center is affected in other nervous ways, or that changes in the accelerator tone also take place. It has been demonstrated that the neighboring centers in the medulla are capable of modifying vagus tone in man. Thus, swallowing is accompanied by a prompt acceleration of the heart, and Pillsbury and Lombard believe that the vasomotor center also affects the cardio-inhibitory center.

Reflex changes in heart rate may also be demonstrated in man. The afferent paths may arise either from the viscera and vascular system or from the periphery of the body. Thus, variations in cardiac rhythm are associated with the degree of gastric distention and with hunger contractions (Carlson), with pressure changes in the aorta (Eyster and Hooker) as well as in the right auricle (Sassa and Miyazaki). In man, such reflexes may be induced from the nose, pharynx and eye. Especially interesting is the *oculocardiac* reflex, first described by Aschner, in 1908, which consists in a slowing of heart rate and sometimes a change in rhythm when the eyeballs are compressed. The reflex is generally supposed to arise from stimulation of the trigeminal nerve. The fact that it occurs in a relatively small percentage of cases has led to the suggestion that it operates only when the vagus tonus is high and has, therefore, been considered as diagnostic of *vagotonia*. It is more probable, however, that, as Levine suggests, it is a normal reflex varying only in different individuals much as other reflexes do. When slowing occurs as a result of this reflex, the beat is initiated at the head of the *S–A* node, or at most shifts to its lower end; but the *A–V* conduction may also be lengthened, especially when the left eyeball is compressed (Levine).[1]

Permanent changes in heart rate may be mediated either through the accelerator or vagi nerves. Slowing of the beat is produced through increased vagus action. Under such conditions, the pacemaker may shift to lower portions of the *S–A* node or to the *A–V* node (Zahn, Meek and Eyster, Schlomovitz, Eyster and Meek) (*cf.*

[1] For additional literature, *cf.* Jour. Am. Med. Assn., 1916, **67**, 1035.

page 52). Acceleration of the heart results either from a decrease in vagus tone or accelerator stimulation. As the accelerator nerves act directly and specifically on the ventricles as well as on nodal tissues, the duration of systole is reduced relatively more than upon removal of vagus control alone (Wiggers and Katz). During such an influence of the accelerator nerves, the *S–A* node may or may not remain the pacemaker (*cf.* page 53). In animals it is possible by simultaneous removal of vagus influence (cutting or atropine) combined with accelerator stimulation to produce exceedingly rapid heart rates when we have every reason to believe the *S–A* node remains the pacemaker. This is shown in Fig. 10, where cycles less than 0.25 second, corresponding to a rate of 240 per minute, were obtained on dogs (Wiggers and Katz).

(*a*) **Sinus Tachycardia.—Nomotopic or Simple Tachycardia.**—Simple forms of tachycardia in which the *S–A* node remains the pacemaker may be either physiological or pathological. Among the former may be classed such accelerations as result from mental or psychic disturbances, exercise, drugs, fever, etc. Their onset is always gradual and the course progressive. They continue as long as the cause is acting. Electrocardiograms show that when acceleration becomes excessive, the relative height of the complexes alters; the *R* and *T* waves become larger, the *P* wave and the *P–R* interval remain practically unchanged. Such tachycardias are normal in every sense. Tachycardia may be regarded as pathological when it is induced by trivial influences, which in normal individuals are without effect on rate. Thus, psychic acceleration is provoked on seeing a mouse or shadow, smelling a disagreeable odor, hearing a shrill noise, etc. Such tachycardias have long been known to neurologists and psychologists as evidences of nervous instability, of which they constitute a sign. Finally, they may arise without evident cause.

Pathological sinus tachycardia may be *temporary*, *recurrent* or *persistent* (Thayer). In the *temporary* and *recurrent* forms, short or long paroxysms may occur in which the heart reaches rates of 180 to 190 per minute. Usually, as in the case reported by White, the onset and offset are not abrupt as in the clinical condition to which the term *paroxysmal tachycardia* seems to have been somewhat arbitrarily restricted (Lewis, Mackenzie, Wedd).

The question as to whether a true "paroxysmal tachycardia" with abrupt onset and offset may occasionally be a sinus tachycardia has recently again invited the attention of investigators. Wenckebach, Galli, Carter and Wedd, Boden and others have reported cases which indicate that such a nomotopic origin is possible. A critical analysis of these cases indicate, however, that either the onset or offset were not demonstrated to have occurred suddenly or the *P* waves of the electrocardiogram may have been misinterpreted. Nevertheless, it would be premature to say that such tachycardias

are impossible (Wedd). If such paroxysmal tachycardias are demonstrated, it will be necessary to assume that a new type of impulse formation suddenly arises within the S–A node, for all experimental work indicates that acceleration produced through nervous or chemical influences is normally progressive and never abrupt (*cf.* Fig. 143). Persistent tachycardia accompanies many disturbances of nutrition or of internal secretion, *e. g.*, Basedow's disease; or it may be a symptom in grave circulatory disturbances, such as hemorrhage, shock and other forms of low blood-pressure, infections and fevers.

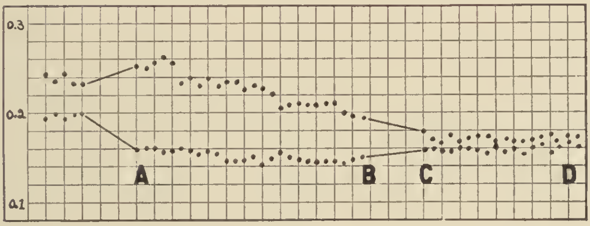


FIG. 143.—Plot showing progressive effect of epinephrin on durations of systole (lower curve) and diastole (upper curve) ordinates, time in 0.1 second. *A*, twentieth beat after epinephrin injection; between *B* and *C*, 45 beats omitted; *C–D*, effects at height of epinephrin stimulation. (After Wiggers and Katz.)

Voluntary Acceleration of the Heart Rate.—Related to recurrent sinus tachycardias are those brought on by voluntary effort. About 16 authoritative cases have now been reported in which individuals possess this rare and interesting accomplishment. In some cases the acceleration appears to be largely due to a removal of vagus tone (West and Savage), but in the majority of cases a direct stimulation of the accelerator mechanism is undoubtedly concerned for coincident with the acceleration there occurs dilatation of the pupil and other phenomena of general sympathetic stimulation (Favill and White, Taylor). Cases investigated show that a rate of 200 per minute may be attained (Favill and White) without any apparent change in the situation of the pacemaker.[1]

(*b*) **Sinus Bradycardia.—Slow Beats of Sinus Origin.**—Sinus bradycardia may be due to intoxication, asphyxiation, anoxemia, drug action or to an increased vagus tone. The condition may occur as a permanent phenomena in old age, during convalescence from febrile diseases, *e. g.*, influenza, typhoid fever, during pregnancy and without known causes. In some cases it is not abolished by atropine

[1] For a consideration of the specific cases, consult Favill and White (Heart, 1917, **6**, 175), Koehler (Arch. f. d. ges. Physiol., 1914, **158**, 579), Pease (Boston Med. and Surg. Jour., 1889, **120**, 525), Tarchanoff (Arch. f. d. ges. Physiol., 1885, **35**, 109), Taylor (Am. Jour. Phys., 1922, **61**, 358), Van de Velde (Arch. f. d. ges. Physiol., 1897, **66**, 232) and West and Savage (Arch. Int. Med., 1918, **22**, 290).

and a toxic effect on the *S–A* node is then indicated. Bradycardia may also be apart of the so-called *vagotonia syndrome, i. e.*, it may be associated with signs or symptoms on the part of other organs which may conveniently be explained by assuming an excessive vagus stimulation (Eppinger and Hess, Blumgarten, Wolfsohn). A slow heart beat of vagal origin accompanies all conditions leading to irritation (mechanical or inflammatory) of the vagus center, its trunk, or its endings, and, finally, may apparently be associated with abnormal reflexes from the viscera, nose or eyeball.

Clinical Recognition.—Clinical bradycardia of sinus origin is usually readily recognized when permanent. The arterial pulse is slow and regular and the jugular pulse retains its normal sequence of waves with the addition of a mid-diastolic wave (*h* wave). The electrocardiogram either shows entirely normal deflections or such variations as are comparable to those demonstrated experimentally as a result of vagus stimulation. Thus, the *P* waves may become flattened or inverted, indicating a shift of the pacemaker to the lower portion of the *S–A* node or *A–V* node. Changes in *A–V* conduction may appear. Thus, when the pacemaker shifts to the *A–V* node the *P–R* interval is shortened, while an effect on the *A–V* bundle tends to lengthen it (Thayer).

The venous pulse and electrocardiogram serve to certainly differentiate these types of slow pulse from those due to nodal rhythm, heart-block, etc. Since compensatory mechanisms operate, permanent bradycardia is not usually associated with a low blood-pressure; on the contrary, the systolic blood-pressure is often elevated.

Vagus bradycardia may also occur as a temporary phenomena when the vagus system is temporarily stimulated. Rarely this results in complete cardiac standstill (Laslett, Gerhardt, Mackenzie); more often it induces only a pronounced slowing, the rate dropping from 40 to 50 per minute. In all of these instances blood-pressure falls rapidly, cerebral anemia occurs acutely and in consequence dizziness, syncope or even epileptic attacks supervene. Periodic recurrence of such attacks are designated as the *Stokes-Adams syndrome,* though this term has more generally become associated with slow cardiac action produced by heart-block. Prolonged standstill of the heart is an occasional cause of sudden death, the literature indicating that if the heart fails to beat for two minutes or somewhat less, recovery does not take place (Lewis).

(*c*) **Phasic Sinus Arrhythmia.**—It is frequently found, especially after digitalis medication, that one or more long cycles are interspersed among shorter ones. This may be so pronounced as to be in reality a temporary standstill. The long cycles may even recur periodically, but then they bear no relation to respiration. Occasionally, the order of emission may be so irregular as to make the radial pulse resemble that of auricular fibrillation (Straubel). These

irregularities are abolished by atropine, hence we may assume that they are vagal in origin and simulate the effects produced in animals by brief vagus stimulation or toxic substances, such as morphine (Einthoven, Eyster and Meek). When variations in length occur from one pulse cycle to the next and these changes are related to the phases of respiration, we speak of a *respiratory arrhythmia*. The acceleration, as a rule, coincides more or less accurately with the phase of inspiration but acceleration during expiration is not unknown.

Clinical Recognition.—The irregular rhythm of the pulse may often be recognized by palpation alone; or the irregular sequence of heart sounds may be heard and its relation to breathing determined. The irregularity may not stop when the breath is held, although its character may be modified. The arterial pulse tracing (Fig. 78, *A*) is characterized by a progressive increase and decrease in the cardiac cycles, the chief variation occurring in its diastole. The waves vary somewhat in size, the smaller ones following the more rapid beats. This is due largely to the fact that the duration of the heart cycle modifies both the systolic and the diastolic pressures within the artery. As the writer has pointed out (page 128) a shortening of a cardiac cycle, as a rule, increases the diastolic and decreases the systolic pressure of the beat following. Conversely, a lengthening of a cycle causes an elevation of the systolic and a fall of the diastolic pressure.

The venous pulse (Fig. 78, *A*) shows a regular sequence of the *a c v* waves with perhaps additional diastolic waves in the long cycles, or the abolition of the *v* wave in the shorter cycles. The *a–c* interval occasionally varies, but we cannot be certain to what extent respiratory variations in venous pressure may account for the change. Hence, it cannot positively be said that the conductivity is impaired through vagus action. The venous record, by showing the *a c v* sequence, is occasionally of service in establishing the nature of this form of irregularity, *e. g.*, when the contraction becomes so premature as to simulate an extrasystole in the arterial record.

The electrocardiogram adds but little information in interpreting this condition. The P, R and T waves show slight variation, probably due to the fact that the position of the heart changes. Sometimes, the P wave periodically flattens or becomes negative (Hewlett). In slow hearts R_1 is larger and T_1 smaller, in the rapid beats R_1 is smaller and T_1 larger. The P–R interval is unchanged or slightly prolonged in the slower beats.

Clinical Significance.—When a phasic arrhythmia occurs during adolescence and follows the phases of respiration no significance should be attached to it. Mackenzie has designated this the "youthful type of arrhythmia" and considers it rather a good omen. Phasic variations of a more irregular character usually have a more serious significance, however. They have been reported in associa-

tion with vagus neuritis (Hoover), vagal tumors (Staekle), meningitis (Rehfisch), increased intracranial tension (Hirschfelder), cerebral lesions and contractions of the foramen magnum (*cf.* Lewis). They are not necessarily indicative of such serious organic disturbances, however, but may merely indicate a highly irritable vagus center, which responds to impulses from neighboring centers or reflexes which are normally ineffective. In this class probably also belong those rare, physiological curiosities who are able to voluntarily stop their hearts.

In *summing up* the significance of sinus irregularities, it may be impressed that they give no evidence of cardiac involvement, but are often a criterion of affections of the nerve supply of the heart. As such, they may be used as an index of nervous function, much as the heart rate variations are used by the psychologist as a criterion of psychical processes.

II. ECTOPIC RHYTHMS.

Clinical Physiology.—Rhythmicity is a function of other portions of the heart besides the *S–A* node. Since the rate of discharge of these subsidiary centers is naturally much slower than that of the *S–A* node and as every discharge from the latter, moreover, dissolves, as it were, the impulses generated elsewhere, it follows that these subsidiary centers can only dominate the rhythm either: (*a*) When the rhythmic activity of a superior node is abolished or held in abeyance, or (*b*) when their irritability is so enhanced that the rate of discharge exceeds that of a superior node. As regards the order of their natural rhythmicity they may be placed in the following sequence: *S–A* node, *A–V* node and *A–V* bundle, posterior portion of auricle, and possibly some portions of the ventricle and Purkinje branches. Rhythms induced in these centers are spoken of as *ectopic* (Lewis) or *heterotopic* (Hering).

(*a*) **Atrioventricular Rhythm (Nodal Rhythm).—Clinical Physiology.**—When the *S–A* node is destroyed by mechanical or chemical means, when its irritability is reduced by cold or by successful effects of vagus influences, the *A–V* node becomes dominant and establishes the rhythm of the heart. Such a rhythm is, however, always slower than the normal. Again, when the rhythmicity of the *A–V* node is enhanced by heat, chemical action or accelerator nerve influences, then it becomes the pacemaker, with the difference, however, that the rate of impulse initiation is now accelerated. Such rhythms have been designated as *homogenetic* by Lewis, since they arise as a result of physiological processes. If, under any of the above-mentioned conditions, the homogenetic rhythm arises in the coronary sinus portions of the *A–V* node, auricular and ventricular sequence remains unaltered; if, however, it originates in the ventricular por-

tions, the As–Vs interval is reduced, abolished or replaced by a Vs–As sequence.

Clinical Recognition.—Most of the reported clinical cases of A–V nodal rhythm are occasioned by a depression or destruction of the S–A node, consequently the heart rate is usually slow (35 to 40 per minute). Occasionally, however, more rapid rhythms occur (Rihl, White, Wilson, Williams and James, Lewis). A–V rhythm occurs after use of drugs (digitalis, atropine) in general myocardial involvement and during febrile diseases.

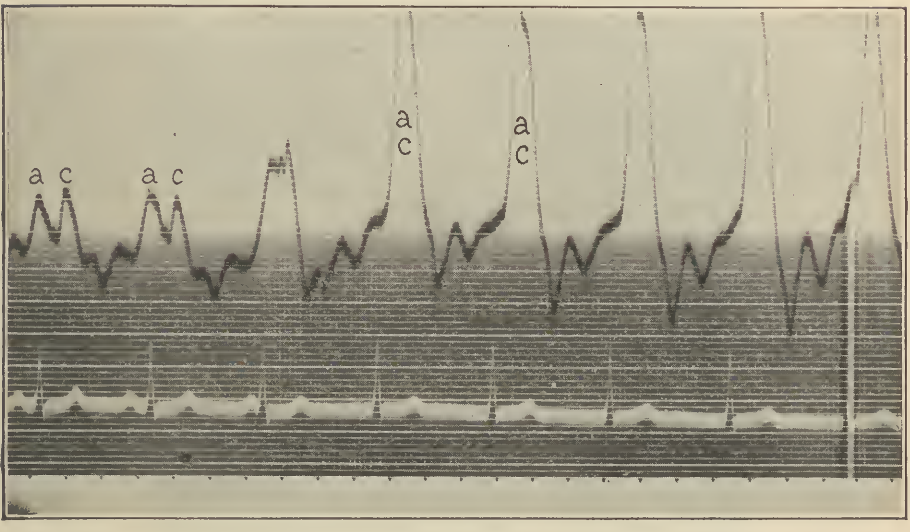


FIG. 144.—Optical venous pulse and electrocardiogram, showing transition from normal to A–V nodal rhythm. Note large regurgitant auricular waves, *a*, *c*, and absence of P wave in electrocardiogram. Auricles and ventricles contract together. (After Hewlett.)

This type of rhythm may occur temporarily, alternate with normal rhythm or may persist for long intervals of time. The former cases are probably due to an excessive nerve action (vagus depression of S–A node or accelerator stimulation of the A–V node); the latter are more probably associated with structural changes to the S–A node. According to the origin of the impulse in the auricular or ventricular portions of the A–V node, three types of cardiac rhythm are produced: (*a*) Auricles beat before the ventricles, but the As–Vs interval is shortened; (*b*) the auricles and ventricles beat simultaneously; (*c*) ventricles precede auricles. Occasionally, the auricles may fail to contract (Frey and Schittenhelm). In the first of these types, the As–Vs intervals are reduced somewhat, consequently both the

a–c intervals of the venous pulse and the *P–R* interval of the electrocardiogram are shortened, but the sequence of waves remains normal with the exception of the *P* wave, which either becomes negative or changes its contour. In the second type, when the auricles and ventricles contract together, the *P* wave is frequently lost in the larger *R* complex of the electrocardiogram, but the venous pulse shows a larger systolic wave, due to the fact that the contracting auricle is unable to empty itself into the ventricle and so causes a

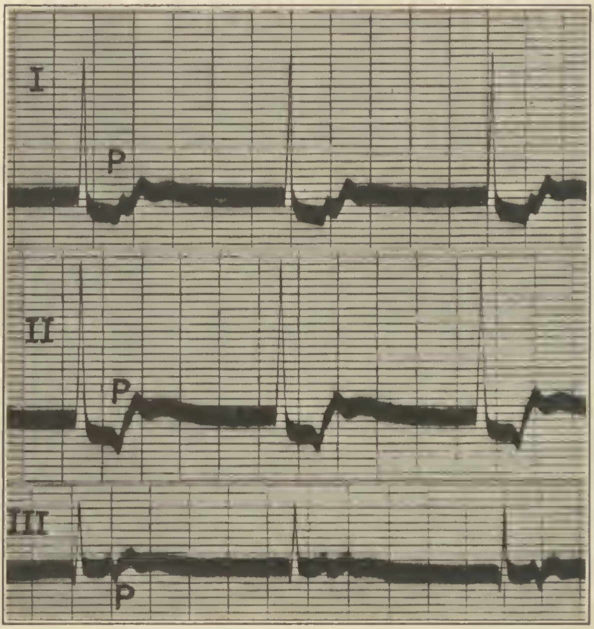


Fig. 145.—Three electrocardiogram leads from case of nodal rhythm, showing reversal of auriculoventricular rhythm. Note incidence of *P* wave after *Q–R–S* complex. (Courtesy of Dr. H. Feil.)

large backward pulse (Fig. 144). In the third class, where a reversed cardiac action occurs, the *P* wave comes after *R*, and the *R–P* interval may then be as great as 0.19 second (Fig. 145) (Williams and James). The reversed beat of auricle and ventricles may be observed fluoroscopically. In some individuals the *A–V* rhythm can be modified by vagus pressure and atropine (White); in other instances, however, this is not possible (Williams and James).

(*b*) **Idioventricular Rhythm.—Clinical Physiology.**—When impulses from the node above the *A–V* bundle are prevented from reaching the His bundle it becomes the pacemaker. Such rhythms have been called *idioventricular*. The rate actually developed is usually slower, although it depends upon the previous rhythm of the ventricle,

being slow if the ventricular rate was previously rapid (Erlanger, Blackman). Consequently, if the normal impulses are rapidly cut off, the *A–V* bundle starts a rhythm which at first is slow and then gradually increases, giving rise to what Gaskell has termed *the rhythm of development*. If on the other hand the ventricles are more gradually cut off, they at once resume their full rate (Erlanger).

Clinical Cases.—As idioventricular rhythms are practically only observed in association with *A–V* block the clinical conditions resulting will be considered more in detail under that heading (*cf.* page 496).

III. PREMATURE SYSTOLES.

(*a*) **Premature Auricular Systoles.—Clinical Physiology.**—The auricle, like the ventricle, is refractory to stimuli applied during the process of contraction. If, however, a stimulus is given during relaxation; both auricles and ventricles respond with a contraction. The rhythm developed by the heart depends, to a considerable degree, upon the region in which stimuli are applied. A stimulus applied near the large veins or near the *S–A* node causes both the auricles and ventricles to respond with premature contractions, then, at an interval almost equal to another beat, both contract normally again. Such premature systoles are sometimes spoken of as *sinus extrasystoles*.

If, however, a stimulus is applied to the anterior surface of the auricle, its premature contraction is followed by a pause somewhat longer than that required for a normal beat.[1] This pause is not so long, however, that the time interval of the two beats quite equals two normal beats (Fig. 78, *C*). The reason that the *S–A* node does not reëstablish the rhythm at the proper time has been attributed by Cushny and Wenckebach to the fact that the extra stimulus is conducted back to the pacemaker and annihilates, as it were, the energy-producing substance without eliciting an actual contraction. It then requires an equal additional interval to rebuild its energy sufficiently to inaugurate a contraction. It is further found that the interval occupied by the two auricular beats is greater than that of the corresponding two ventricular contractions. This has been assigned to the fact that the longer rest following the premature systole causes a reduction in the conduction interval from the *S–A* node to the ventricle.

The fact that the interval occupied by a normal plus a premature systole of the ventricle is equal to less than two beats, is used to distinguish premature systoles originating in the auricle from those originating in the ventricle. The degree of shortening of the ventricular beats, however, depends also on the phase of auricular diastole in which the premature contraction is called out. Thus,

[1] Actually this interval is longer by an interval exactly equal to the time consumed by it in passing back to the S–A node.

Hirschfelder and Eyster found that while the interval occupied by two ventricular beats was always less than that of two normal beats when a premature contraction was called out early in auricular diastole, the same interval very nearly equaled two normal beats when the auricular premature contraction took place late in diastole.

Under certain conditions a premature contraction of the auricle may take place without a corresponding ventricular beat. This happens: (*a*) When the extra-stimulus is blocked and for some reason fails to reach the *A–V* node; (*b*) when it reaches the ventricle during its refractory stage; (*c*) when the abnormal and normal impulses annihilate one another (de Boer).

Clinical Recognition.—It is evident from the experimental analysis:

1. That in the majority of cases the period of premature contraction of the auricle plus a normal contraction equals less than two auricular periods.

2. That the premature response of the ventricle plus a normal beat usually equal an interval less than two normal periods.

Cases of such a simple nature can be diagnosed by simple methods. The arterial pulse is usually characteristic, if carefully studied (Fig. 79, *C*). The regular rhythm is interrupted by a small wave or an intermission, as in ventricular premature contractions. It differs from this condition in that the interval following is not sufficiently long so that it together with the preceding beat equal two normal pulse lengths; that is, in the case of auricular premature contractions we get a *shortened bigeminus*. It is further possible to determine whether the premature contractions arise near the sinus region or in some other section of the heart. In *sinus extrasystole* the distance from the beginning of the premature contraction to the next normal beat equals a normal beat in length. This is not the case in premature systoles arising in other portions of the auricle.

The venous pulse (Fig. 78, *C*) shows throughout a normal *a c v* sequence. Where the premature contraction occurs an *a c v* group also appears prematurely. The *a–c* interval is usually increased in this group, partly because the isometric period of contraction is prolonged and the opening of the semilunar valves delayed. The electrocardiogram is supposed not only to establish the presence of premature systoles, but also to give further evidence as to the region of the auricle in which they arise. In the simplest cases there is merely an early occurrence of a normal *P–R–T* complex. The *P* wave may be superimposed on a preceding *T*, making it larger or notched. Occasionally, it is negative or diphasic (Fig. 146) and again it may be absent. It is often better recognized in Leads II and III. Experimental work has indicated that the nature of the *P* wave is determined largely by the region of the auricle from which the stimulus arises (Lewis, Ganter and Zahn). Thus, while a systole arising in the sinus region gives a premature *P* wave of normal form, those arising in the region of

the coronary sinus or in the auricle show a negative P wave, presumably because the impulse spreads in the opposite direction. According to Lewis, most electrocardiograms from patients give evidence of a negative wave and so indicate that the stimuli arise in some region of the auricle aside from the normal pacemaker (Lewis). Since the ventricular complexes R, S, T are normal, it must be inferred that the premature stimulus reaches both ventricles simultaneously.

Not all premature auricular contractions are followed by such normal R–S–T complexes in the electrocardiogram, however. Undoubtedly, this occurs because disturbances of conduction, due either to organic changes or to insufficient rest, are often present in these cases. The chief variations met with are: (*a*) Complexes resembling those arising from a premature contraction of the right ventricle (*cf.* Fig. 100), or (*b*) those arising when the branch to the left ventricle is cut (Hoffmann). This may be explained by assuming that a conduction disturbance is present and the stimulus is propagated to the right ventricle before passing to the left. Finally, when total block occurs the entire ventricular complex may be absent (Hewlett).

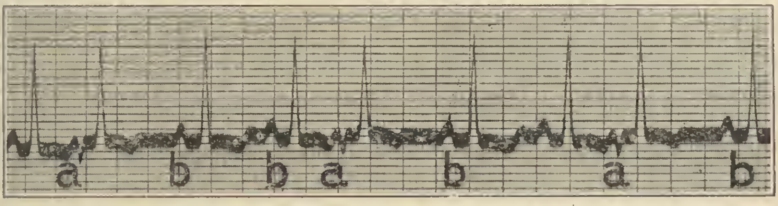


FIG. 146.—Electrocardiogram, Lead II, showing premature auricular contractions arising in abnormal focus. *a*, premature complexes; *b*, normal complexes. (Courtesy of Dr. R. Scott.)

It is apparent, therefore, that electrocardiograms of premature auricular contractions may, on account of simultaneous conduction disturbances, resemble, on casual examination, those arising in the ventricle. This is especially so when, in addition to the "aberrant" complexes, the P wave is obscured by the preceding T wave.

(*b*) **Premature Contractions of Nodal Origin.—Clinical Physiology.**—Experimental work has shown that if the tissue of the A–V junction is stimulated a series of premature contractions occur simultaneously in auricle and ventricle. Such simultaneous beats of auricles and ventricles have also been found in cases of aconite poisoning (Cushny) and after ligation of a coronary branch (Lewis), and the assumption seems justifiable that in these cases the impulse arises somewhere in the junctional tissue. Owing to the fact that the impulse may reach either the auricle or the ventricle first, it usually happens that the contractions are not absolutely synchronous, but that merely a reduced As–Vs interval, or, in case the ventricle

contracts first, a short *Vs–As* interval occurs. This interval is not necessarily reduced when the impulses originate at the *A–V* node—in fact, such a shortening occurs experimentally only in those cases in which the impulse originates in the ventricular portion of the node (Zahn).

Clinical Recognition.—The diagnosis of this condition in man hinges largely upon establishing the existence of a reduced *As–Vs* interval, the entire abolition of this interval or the actual presence of a *Vs–As* rhythm. In this capacity the arterial pulse is of no value, for it presents a picture of a ventricular premature contraction with a somewhat shortened compensatory pause. According to Mackenzie and Lewis, the condition may be more than suspected: (*a*) When the *a* and *c* waves fall together so as to produce a bifurcated systolic wave; (*b*) when the *a–c* interval is appreciably reduced (Mackenzie, Wenckebach); (*c*) when the *a* wave definitely follows the *c* wave.

Too great caution cannot be urged, however, in such interpretation, for lever oscillations of polygraph tambours or premature ventricular systoles may similarly produce such summated or notched waves; and respiratory variations of venous pressure may apparently reduce the *a–c* interval. Furthermore, according to Volhard, the occurrence of an *a* wave after a *c* wave may result from a retrogression of a ventricular impulse. Finally, we cannot always be certain as to what waves are due to auricular systole.

The electrocardiogram shows a normal ventricular complex, *R–S–T*, which indicates that we are not dealing with a ventricular premature systole as might be inferred from the carotid. The *P* wave is abnormal, owing to the opposite direction of the impulse. Its character is usually best seen in Leads II and III (Hoffmann), where it often appears as an inverted or negative wave. Frequently, the most conspicuous feature is the abnormal position of *P;* it may precede *R* by a very short interval or be superimposed on the *R* wave, in which case it may cause a deep *S* depression. The location of the *P* wave may vary in the same subject, indicating a shifting of the pacemaker between the auricular and ventricular portions of the *A–V* node.

(*c*) **Premature Ventricular Contractions.**—**Clinical Physiology** (Fig. 147).—If a mechanical or electrical stimulus is applied to the normally beating ventricle of any vertebrate animal (man included) during its diastolic phase, the ventricle will respond with a "premature" or "extra" contraction. If a similar stimulus is applied during its contraction, however, no response is given. When a contraction is prematurely called out by an external stimulus, the total number of beats is not increased, as a rule, but this premature beat is followed by a pause of such length that it plus the preceding contraction equals approximately an interval of two heart beats (Knoll). This *compensatory pause*, as it is termed, exists because the normal sinus

impulse, which should evoke a ventricular contraction, reaches the ventricle during the refractory phase of the premature contraction. The next ventricular contraction does not occur until the following rhythmic stimulus from the S–A node arrives. Careful measurements have shown, however, that this compensatory pause is not always exactly equal to two normal periods, but that it often falls short of this. This is probably due to the fact that the sinoventricular conduction has improved during the long rest, making the contraction premature. The postcompensatory ventricular systole following the beat prematurely called out is usually larger than normal and accounts in part for the larger pulse beats.

It is evident that in the above cases there is no beat gained by the heart; hence, the term *premature contraction* seems preferable to *extrasystole*. It may happen, however, that true extracontractions or "interpolated" systoles occur. Thus, when the cardiac rhythm

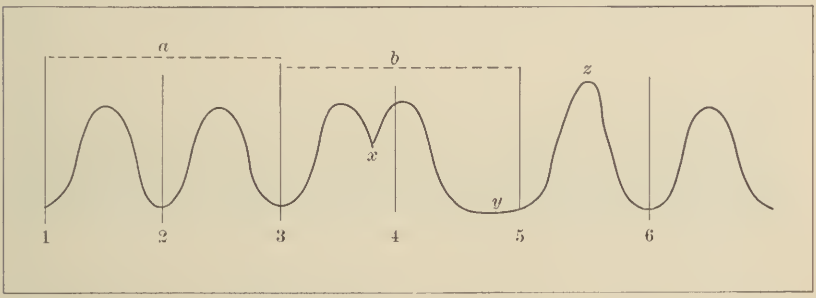


FIG. 147.—Diagram illustrating the nature and cause of the compensatory pause after a premature contraction. Lines 1, 2, 3, etc., represent time of arrival of natural impulse; x, premature contraction in refractory phase of which normal impulse, 4, falls. Periods a and b are equal.

is very slow and the premature contraction is elicited early in diastole, the ventricle may have passed its refractory phase before the next regular sinus impulse arrives.

It has been implied that premature excitations in the ventricle are not propagated backward through the A–V bundle to excite a corresponding auricular beat. Indeed, it has often been supposed that this unidirectional conduction of the junctional tissue accounts for the continuance of the S–A rhythm and the compensated ventricular rhythm.

The cause of this unidirectional conduction has long been under discussion and was at one time considered a strong argument in favor of nervous conduction. More recent work indicates, however, that impulses *are* actually conducted, but fail to elicit a response because they arrive during the refractory phase of auricular contraction (Lewis).

Clinical Recognition.—Premature systoles of the ventricle may frequently be diagnosed by auscultation of the heart sounds alone. Optical records (Lewis, Gerhartz) indicate that effective premature contractions cause two sounds. The first sound is of shorter duration and smaller amplitude (35 per cent less) but of the same vibration frequency as the normal sound. The second sound is also of smaller amplitude (10 per cent less) and shorter duration, but is said to be of higher frequency than the normal. Gerhartz quotes a case in which the first sound lasted 0.257 second (normal 0.461 second) and the second sound 0.095 second (normal 0.138 second). When the semilunar valves are not opened only a single sound is recorded.

In the main, these records corroborate the auscultatory findings. The regular sequence of sounds is interrupted by two short sharp sounds or by only a single sound if the systole is ineffective. According to Mackenzie, it may be accepted that such a sequence during a pulse intermission or small wave is due to a premature contraction. The only confusion arises in cases of partial block with mitral stenosis, in which a sound due to the contraction of the auricle may occasionally be produced, but in these cases the presystolic murmur helps to differentiate.

The arterial pulse (Fig. 78, *B*) is distinctive. The regular rhythm is interrupted by a premature small wave or the absence of a wave and a long pause. The characteristic feature, pointed out by Cushny and Wenckebach, consists in the fact that the small contraction and the compensatory period following are equal approximately to two normal cycles, a form of pulse to which the term *full bigeminus* has been applied. The compensatory period is followed, as a rule, by a wave of larger amplitude. This is due to the larger pulse pressure, which results in part from the stronger systole, in part from the more complete diastole following and in part from the lower diastolic pressure existing at the time. It is generally stated that an interpolated systole causes a trigeminal wave group equal to two normal cycles. Actually, however, the third beat rarely causes a radial pulse and, when rhythmically repeated, such instances may suggest alternation (Dresbach and Mumford, Laslett, Myers and White).

The venous pulse is often characterized by the occurrence of a premature *c* wave at the time of the premature systole. This is followed in its proper sequence by an isolated wave that may be attributed to subsequent auricular contraction (*a* wave).

The place of origin of the ventricular premature systoles cannot be determined exactly by any of these procedures. It may be suspected with a fair degree of certainty in some cases. Thus, in cases of high arterial pressure or in aortic insufficiency we may surmise that the stimulus arises in the left ventricle; whereas, in mitral lesions the suspicion is directed toward the right ventricle (Hirschfelder).

A more approximate localization of the heterogenetic focus may be

made by the aid of the electrocardiogram. Kraus and Nicolai were the first to observe that a premature contraction elicited from the upper portion of the heart or right ventricle causes a positive variation, followed by a negative wave (Type A); whereas, one elicited near the apex or left ventricle causes a prominent negative variation followed by a positive variation (Type B). While these results are apparently correct, the interpretation of different wave forms occurring in ventricular premature contractions has not proven as simple as was at first supposed (*cf.* Kahn, Lewis, Rothberger and Winterberg). The established facts are as follows: (1) When the major deflection is directed downward in Lead III, the focus is in the left ventricle; (2) when it is directed upward in Lead III and occasionally downward in Lead I, it is of right ventricular origin (*cf.* Figs. 100 and 148); (3) the contour of the deflections varies with the portions of the respective ventricles from which they arise. Cohn has recognized eight more or less common types in man. These range from those frankly of right or left ventricular origin with many intermediary forms.[1]

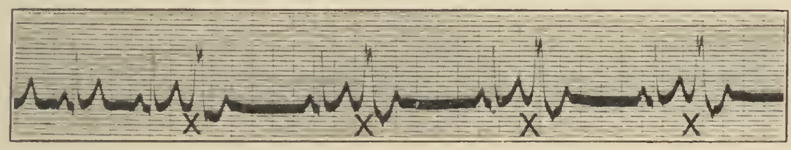


Fig. 148.—Electrocardiograms (Lead II) from patients with recurrent premature ventricular systoles. Abnormal aberrant deflections arising in right ventricle are indicated as *X*. (Courtesy of Dr. R. Scott.)

Experimental work has shown that stimulation of the same area, without exception, causes complexes of identical contours, so that we can interpret with certainty the uniform origin of excitation by the similarity of complexes.

Occasionally, premature contractions may arise with great regularity in relation to normal beats, thus producing regularly coupled beats as shown in Fig. 148. The arterial pulse then takes on a bigeminal type which suggests alternation. From this it may be distinguished, however, by the fact that the smaller beat is of longer duration (*cf.* page 508).

IV. PAROXYSMAL TACHYCARDIAS.

Paroxysmal tachycardia is a condition in which showers of premature excitations arise abruptly in ectopic centers of the heart and by dominating the cardiac rhythm cause rapid heart action. The

[1] For comparison with electrocardiograms taken from dogs, when different areas of ventricular surface were stimulated, see Lewis (Phil. Trans. Roy. Soc., London, 1916, pp. 207 and 279).

paroxysms may consist of only a few beats or they may persist for days and weeks, terminating as abruptly as they started. According to their origin, three types are recognized, viz.: (*a*) Auricular, (*b*) atrioventricular and (*c*) ventricular.

(*a*) **Auricular Tachycardia.—Clinical Physiology.**—If the auricles in experimental animals are stimulated by repeated induction shocks, the frequency of which is above that of the normal rhythm,[1] both auricles and ventricles respond to the rate of this artificial pacemaker. The abnormal rhythm starts with a few premature beats and, when stimulation ceases, is followed by a pause before the normal rate is restored.

A corresponding condition has long been recognized clinically. Suddenly and without warning the heart beats at rates varying from 120 to 180; often the original rate is exactly double. These attacks are accompanied by some respiratory distress and extreme exhaustion. The rhythm of the heart is extremely regular (Feil and Gilder) and is affected neither by posture, rest nor exercise (Carter and Wedd). Some cases are affected by vagus compression, not in the sense, however, of moderating the rhythm gradually, as in normal individuals, but in abruptly restoring the normal rhythm. This can best be explained by assuming that the vagus depresses an irritable center, so that it no longer discharges and, in consequence, the normal pacemaker again dominates the rhythm.

Clinical Recognition.—Clinical recognition is usually easy without graphic procedures; these, however, make the auricular origin more certain. The arterial pulse presents the typical picture of a paroxysmal attack ushered in by a few premature contractions of auricular origin and followed by small contractions at a very rapid rate. The venous pulse, likewise, shows that, at the inception of an attack, the regular rhythm is first interrupted by premature contractions of auricular origin. Later, the normal sequence of *a–c–v* waves may be retained, but if the pulse becomes too rapid the *a* wave replaces the *v* wave, which may then be mounted on the descending limb of the *c* wave (Fig. 79, *D*). It is precisely in cases of such rapid action, however, that the ordinary polygraph tambours introduce the greatest errors through lever fling and the addition of excessive waves; consequently, they cannot be expected to follow the changes in the venous pulse exactly.

The electrocardiogram gives evidence that the introductory premature contractions and paroxysmal beats arise in identical areas, for the *P* waves are similar in form. In intervals between paroxysms, the *P* wave may retain the characteristics shown in paroxysms (Fig. 99). The ventricular complexes differ from the normal only in that the *P* wave is often superimposed upon a preceding *T* wave.

(*b*) **Atrioventricular Tachycardia. — Clinical Physiology.** — Under exceptional conditions the *A–V* node in man may abruptly become

[1] The rate must not exceed approximately 300 per minute.

the pacemaker and cause a tachycardia. It can, as yet, not be definitely stated whether these conditions fundamentally correspond to those experimental tachycardias resulting from stimulation of the left accelerator nerve (Rothberger and Winterberg, Clere and Pezzi), or whether they are due to a pathological disturbance at this node, which results in raising its irritability. Clinically, nodal tachycardias are rare, a total of about 8 cases having been reported (Fussell and Wolferth). As in junctional premature systoles, the auricles and ventricles contract absolutely or approximately together.

Clinical Recognition.—The attacks quite closely simulate those of auricular origin, from which they are distinguished only by a study of the electrocardiograms and venous pulse (Fig. 144). The arterial pulse is at all times small and again large and dicrotic (probably because of imperfect recording sphygmographs). The jugular pulse is characterized by systolic elevations, due to the fact that the auricle during its contractions empties into the veins (Fig. 144). Many of the published records, however, are clearly arterial tracings from the neck. The electrocardiogram usually best serves to differentiate nodal from other forms of tachycardia, but under many conditions difficulties arise which render their interpretation difficult (Wedd). When the *P* wave is inverted or either precedes or follows *R*, and when the ventricular complexes remain normal (Fig. 145), the origin of the focus is readily established. When the *P* wave fuses with *R* and causes certain deformations, the interpretation may become less certain (Fig. 144). In such instances, supplementary records of the venous pulse, which show large summated *a* and *c* waves during systole, may be more valuable than electrocardiograms; indeed, it is on the basis of such tracings that the condition was originally recognized (Rihl). Meakins has undertaken an experimental study to determine the shape of the electrical auricular complex during nodal rhythm and finds it variable. As a rule, it starts in a downward direction or may be entirely downward. The abrupt nature of the onset and offset is especially important in diagnosis. Often no carotid pulse is felt upon cessation of this form of tachycardia, but the galvanometer string undergoes violent oscillations.

(*c*) **Tachycardias of Ventricular Origin.**—**Experimental Physiology.**—It has been demonstrated by Lewis that a series of extrasystoles may be elicited from the ventricles of experimental animals, thus giving the effect of a tachyrhythmia of ventricular origin. When the ventricle is stimulated by repeated and accurately spaced electrical stimuli, they are at first only periodically conducted back to the auricle, and so call out only irregular auricular systoles. Gradually, however, the conduction is improved, so that more and more premature contractions occur, until at last the auricle may accurately follow the pace set by the ventricle. Similar results have been obtained by tying the coronary artery (Lewis), by stimulation, after poisoning

the heart with Ba or Ca, and, also, by combined stimulation of accelerator and vagus nerves (Rothberger and Winterberg; Ken Kuré).

Clinical Recognition.—The condition differs from other tachycardias by persisting for a shorter time, usually for from six to thirty beats (Cohn, Hart, Lewis). Lewis reports a case lasting five minutes, which is apparently the maximum period reported.[1] The rate may be as high as 300 per minute. The attacks also recur frequently.

The venous pulse shows a complex mixture of *a* and *c* waves, and those so far recorded seem of little value in differentiating the condition. Even the electrocardiograms are sometimes uncertain in determining whether or not auricular contractions exist, but the fact that retrograde conduction occurs can no longer be doubted (Lewis, Hart, Scott) (Fig. 149). According to the origin of the ventricular stimulus, as indicated by the electrocardiogram, these disturbances may be divided into two classes: (*a*) Those in which premature contractions arise in the right ventricle; (*b*) those in which they arise in the left ventricle. As may be anticipated, the characteristic feature consists of six to thirty wave groups resembling complexes characteristic of right and left ventricular premature systoles (*cf.* Figs. 100 and 148). In a third group, mixtures of the two occur.

An example of the onset and effect of such a paroxysm of the right basal type is shown in Fig. 149, taken by Lead III. The first beat is clearly a premature one and is followed by others similarly recurring at a rate of 240 per minute. The notch on the descending limb is probably a *P* wave, due to reverse conduction, but in some cases retrograde conduction is apparently absent (Lewis). Between paroxysms the ventricular beats are often arranged in groups, so that normal and premature complexes alternate (Fig. 148).

Factors Concerned in Production of Premature Systoles and Paroxysmal Tachycardia.—Many experimental and clinical facts make it reasonably certain that paroxysmal tachycardia essentially represent showers of premature extrasystoles and, therefore, point to the probability that the same fundamental causes and processes underlie both conditions. Our conceptions as to the nature of these disorders in man has largely been molded by the fact that both conditions may be experimentally reproduced by the application of single or repeated stimuli (mechanical and electrical) to the heart. While, undoubtedly, certain clinical premature systoles of ventricular origin may logically be attributed to a sudden application of extraneous stimuli to perfectly normal hearts (*e. g.*, sudden increase of aortic pressure, pressure of diaphragm upon heart, changes of intrathoracic pressure), such an explanation does not readily explain paroxysmal showers of such contractions.

The suggestion that certain areas in an otherwise normal heart

[1] Recently Scott has reported a case in which one of the recurring paroxysms lasted for forty-eight hours (Heart, 1923, **9**, 297).

may have their irritability so augmented through nervous influences that they are capable of emitting impulses, also lacks experimental

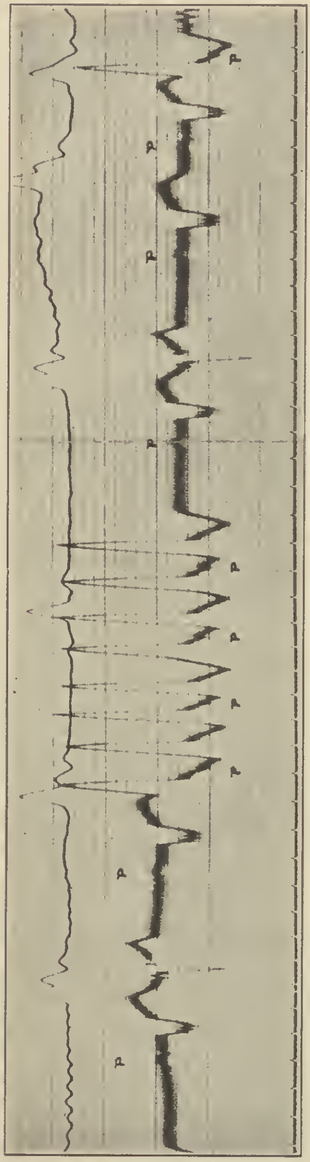


Fig. 149.—Radial pulse and electrocardiogram (Lead III), showing short paroxysms of ventricular tachyrhythmia and two types of premature ventricular contractions. Notch on descending limb of *R* interpreted as *P* wave. (After Stuart Hart.)

proof. While it has been reported (Rothberger and Winterberg; Ken Kuré) that simultaneous vagal and sympathetic stimulation may

produce premature contractions, the instances occur so rarely that they may well be assigned to accidental causes (Lewis). Since they are much more readily induced, however, when the heart is poorly nourished or subjected to toxic influences (Ba, Ca, chloroform) (Rothberger and Winterberg, Levy), it seems probable that nervous influences may indeed initiate attacks, provided hearts are abnormally irritable. It may be assumed in these cases either that the irritability of the heart is increased through toxins, internal secretions, caffein, nicotine, etc., so that it reacts to tiny, normally ineffective stimuli that bombard it; or, that pathological disturbances of structure are actually present. When they occur in advancing age, after infections and in association with hypertrophy and valvular lesions, we should incline to the latter diagnosis.

Linked with this idea is the hypothesis that so-called irritable foci (or a single irritable focus) develop in the heart and become more or less rhythmic (Hering, Lewis). So far, however, demonstrable pathological changes have not been localized in localities where premature systoles originate, nor has any explanation been offered as to why a toxemic or nutritional disturbance should periodically affect only a single focus. It is probable, therefore, that while nutritional and toxemia conditions may have a casual relation to the production of a series of premature beats, they do not represent the fundamental mechanisms initiating them.

A hint as to a possible physiological mechanism has been suggested by the work of de Boer. This investigator found that a single extraneous stimulus applied to a poorly nourished frog's ventricle may produce: (*a*) A single premature contraction when applied late in diastole; (*b*) a series of premature beats when applied a short time after the end of the refractory phase; (*c*) fibrillation when it is applied immediately at the end of this phase. This investigator, therefore, believes that, in this condition, the refractory period is shorter, the excitation wave is conducted more slowly and, as a result, a circus movement is set up much as in the case of auricular flutter and fibrillation (*cf.* page 474). While these conceptions require further substantiation, we must be prepared to abandon entirely the conception of a rhythmic punctate focus and substitute for it the phenomena of a circus movement, as has recently been necessary in the case of flutter and fibrillation. In such event, it would require only a single extraneous stimulus at the proper moment of relaxation to account for tachycardial paroxysms.[1]

Further speculation may be made as to why an irritable focus or a circus ring may sometimes only emit an occasional impulse and again a perfectly regular series resulting in tachyrhythmia. Of

[1] The observation of R. W. Scott that quinidine may abolish a persistent paroxysmal tachycardia of ventricular origin would lend circumstantial support to such an interpretation. (Heart, 1923, **9**, 297.)

interest in this connection is the hypothesis of Kaufmann and Rothberger that many premature systoles owe their existence to the fact that a second rhythmic center (or ring?) may operate simultaneously with a normal pacemaker, because it is "block protected" from impulses of S–A origin. When such a center (or ring?) develops a rhythm more rapid than that of the normal pacemaker and sends these to the heart, it becomes the pacemaker and dominates the rhythm. If, however, regular or irregular blocks arise, only an occasional impulse reaches the rest of the myocardium and, consequently, premature systoles result. Nine cases of premature systoles, recurring at apparently irregular intervals, have been reported in which the intervals between these abnormal systoles not only have a common divisor less than that of the normal cycle, but in which grouped premature contractions were present at intervals also corresponding to this divisor. This type of rhythm has been designated as *pararhythmia* (Kaufmann and Rothberger). The plausibility of this conception is enhanced by the experimental observations of Kisch, that in dying rabbits auricular contractions involving only parts of an auricle (*partial extrasystole*) may be interpolated between regular beats, owing to failure of excitations to reach the normal pacemaker and so extinguish the succeeding impulse.

Prognosis.—The prognostic significance of premature systoles is as yet not determinable. Probably a large percentage of normal individuals are subject to occasional premature contractions, and it has not been possible to differentiate such apparently normal phenomena from those due to toxemia or structural defects of the heart. Similar statements apply to paroxysmal tachycardia. They may persistently recur for years, and the discomfort attending the attacks may be the only handicap these patients have. On the other hand, they may pass into ventricular fibrillation and be the cause of sudden death. The prognosis apparently depends upon: (*a*) Whether it is the only myocardial affection, and (*b*) whether they are of ventricular or auricular origin, the latter being considered more serious.

V. AURICULAR FLUTTER AND FIBRILLATION.

Physiology.—If a dog's auricle be briefly stimulated with induction shocks of high frequency, one of three conditions may persist for short periods of time after removal of the stimulating current: (1) The auricles may beat coördinately and absolutely regularly at rates of 345 to 580 per minute. To this mode of reaction the term *auricular flutter* should be restricted (Lewis and associates). (2) The auricles may beat rapidly and coördinately, but not with absolute regularity, giving rise to a condition termed *impure flutter*. (3) A condition of *fibrillation* may develop—a state in which rapid, irregular and apparently incoördinated twitchings appear over the entire

auricular surface or occasionally these may merge into small wavelets traveling short distances over the auricular surface. According to Lewis and his associates, two distinct types of auricular disorder have been included in this category of "experimental auricular fibrillation," viz.: (*a*) A condition, essentially an advanced stage of impure flutter and identical with "*clinical fibrillation*," in which 400 to 600 excitation waves spread over the auricle in orderly succession, but not at equal or constant rates; (*b*) "*rapid reëxcitation*," a disorder as yet unrecognized as a pathological clinical state in which small tremulous movements in a distended auricle are produced by excitation recurring at extremely rapid rates (1000 to 3500, Lewis and others) (3000 to 3500, Rothberger and Winterberg).

During the states of pure and impure flutter, the ventricles rarely respond to every auricular beat, but more commonly a form of regular or irregular block is produced. Thus, the ventricles may adopt a regular half- or quarter-rhythm; in other cases, the ventricles beat

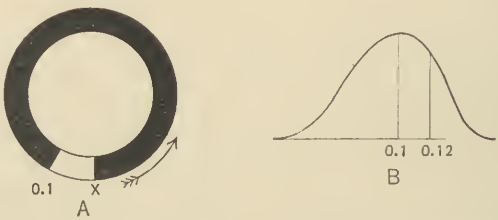


FIG. 150.—Two diagrams elucidating the mechanisms of circus movements. Discussion in text. *B*, assumed contraction curve of any fraction of the ring shown in *A*, *e. g.*, of *X*.

at irregular times, yet always in relation to an auricular beat. In auricular fibrillation the ventricular responses are rapid and so exceedingly irregular as to give to the observing eye the appearance of hopeless confusion in rhythm and amplitude—a condition which has led early investigators to designate it as *delirium cordis*.

What initiates and determines the continuance of such excitations? As in ventricular tachycardia and fibrillation, it was long supposed that the impulses arise from a single irritable focus. More recent experimental work (Mines, Garrey, Lewis and associates) indicates, however, that the excitations arise from a self-perpetuating ring of excitation in the auricles. Let us suppose, for instance (Fig. 150, *A*), that a ring of muscle is stimulated at *X* at a time when a block exists just to the left of the point stimulated. Under such conditions the impulse spreads in a counter-clockwise fashion only. As each portion of tissue is excited a local excitation and contraction result, lasting say 0.1 second.[1] During this phase the muscle is refractory. If the

[1] *Cf.* Fig. 150, B

rate of conduction around the circle is less than 0.1 second, the returning excitation will strike the muscle at X in a refractory phase and thereby annul itself. If, however, the rate of travel is such that it requires more than 0.1 second to complete the circle, it will find each muscle fraction responsive again (Fig. 150, B), and the wave continues as long as a gap exists between the advancing excitation wave and the refractory tissue.

Since it is essential for the continuance of such a circus excitation that the wave should not complete the circle before the refractory phase of the muscle first excited has passed off, it is obvious that three factors are concerned in the production of circus movements, viz.: (1) The length of the path, (2) the rate of conduction, and (3) the length of the refractory phase itself. Calculations have shown that as long as the conduction rate and the refractory phase remain normal in auricular tissue, circus movements cannot develop unless the rings are more than 200 mm. in circumference (Lewis and associates). Since actually these rings are much smaller, however, it is necessary to assume that either the conduction rate is reduced or the refractory phase is diminished in experimental auricular fibrillation. As both of these results are established when the heart is rapidly excited, it has generally been supposed that they jointly contribute to the production of circus movements (Rothberger and Winterberg). Lewis and his associates have submitted evidence which seems to indicate that the reduced rate of transmission is not caused by depressed fiber conduction but by the fact that, under rapid excitations, certain muscle fractions remain refractory at the time an impulse strikes them. The excitations are, therefore, required to detour through other and more sinuous paths, which has the effect of delaying their movements around a circle. The probability, therefore, exists that the alterations of the refractory phase are *solely* responsible for the phenomena of circus movements.

According to this exposition of the nature of circus excitation first developed by Mines, it is necessary to assume that a unidirectional block exists. Both Mines and Garrey obtained evidence of the existence of such a local block, but failed to explain its origin. It is not necessary, however, to assume the existence of a unidirectional block when circus movements are established as a result of stimuli repeated at rapid rates (Lewis, Drury and Bulger). Under these conditions a state of partial refractoriousness develops (*cf.* page 37), which periodically causes a local but absolute block. If the artificial stimuli happen to be withdrawn at this moment, it follows that by the time the excitation next to the last has completed the circuit it finds this portion responsive and the excitation continues in a circuit.

The recent researches of Lewis and his associates (1918–1921) have definitely shown, moreover, that, in fibrillation and allied dis-

orders, only a single circus ring is established and maintained, and that from this *central* or *mother ring*, centrifugal waves spread to the more outlying regions of the auricle (Fig. 151). According to this work, it appears that different fractions of auricular tissue are not excited in hit-or-miss fashion, but that, on the contrary, the centrifugal excitation waves leaving the central circuit spread in fairly definite and orderly paths to surrounding auricular tissue. In other words, as regards order of excitation, the auricular beat is not incoordinated. The details of these phenomena may now be considered in the various types of flutter and fibrillations defined above.

Pure Auricular Flutter.—Tracing the pathway of impulses across the auricle by the use of paired electrodes, Lewis and his associates found that the incidence of excitation of various points over the auricle is changed from that normally found (*cf.* page 31), but is

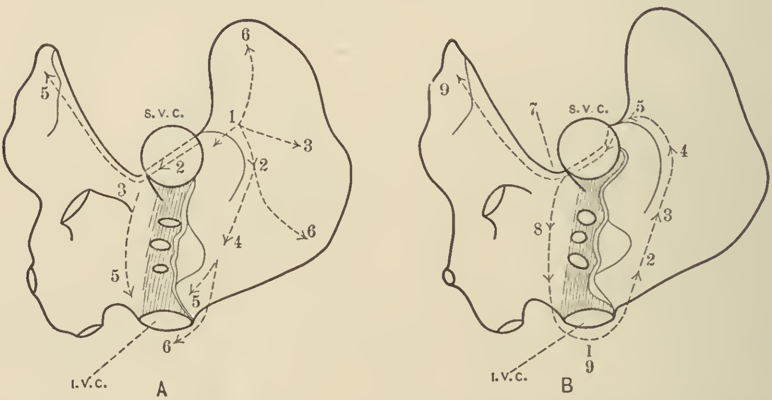


Fig. 151.—Diagram of posterior portion of auricle. *A*, showing order of excitation when impulse spreads normally from *S–A* node to right and left auricles. *B*, showing order of excitation in circus movements during flutter. (After Lewis.)

so related that a definite central circus path can be established (*cf.* Fig. 151, *B*). Thus, the earliest excitation wave often begins at the inferior vena cava, 1, instead of at the *S–A* node, as normally. Following the order of excitation, it is found that the impulse travels up the entire length of the tenia, 2–5, moves around the superior vena cava across the interauricular band, 6–7, to the left auricle. Thence it passes downward, 8, and back to its start, 9, at the inferior vena cava. All experimental evidence is contrary to the idea that impulses arise *de novo* from this point, but support the view that the impulse reënters the circuit at 1 (*reëntrant path*) and establishes a circus movement. From this central or *mother path*, which gives the tempo to the auricle, offshoots or centrifugal excitation waves pass to the more peripheral tissue of the auricle. Thus, as shown in Fig. 151, *B*, the impulse may reach the left auricular appendage at the same time that it returns to the inferior vena cava. It can readily

be seen that this produces a condition where some fractionate contraction is always going on and in which, strictly speaking, the auricle, as a whole, has no true diastole (Lewis and collaborators). Nevertheless, the varying balance of contraction and relaxing fractions is such that the auricle, as a whole, still has alternating phases of shortening and lengthening (Wiggers), to which, according to our definition (page 70), the terms systole and diastole may still be applied.

Impure Flutter.—The experimental work of Lewis and his associates has also shown that a similar circus excitation underlies and is the fundamental cause of impure flutter. There are these differences, however, in various forms of impure flutter: Owing to varying blocks (*i. e.*, areas still in the refractory phase) interspersed in the path of the centrifugal waves, local deflections of the excitation waves take place which produce irregularities in the response of the auricular muscle. As the central path is unaffected, these irregularities are, in a sense, compensated as regards rhythm. This simple type of impurity shades through many transitional types into a variety where the excitation waves are deflected in the central path itself. When this occurs the rates become more and more irregular and merge almost imperceptibly into the condition described as *clinical fibrillation.*

Clinical Fibrillation.—When the central excitation ring is blocked so frequently and so irregularly that the impulse must trace its path continuously through a sinuous path, the circuit can obviously not be completed within times that are even approximately regular; consequently, the tempo of the auricle is very irregular. This obtains in clinical fibrillation. As the rate of auricular excitation is much greater than in flutter, and as this acts further not only to abbreviate the refractory phase but decreases also the period of response (*cf.* Fig. 6), it must mean that the central path in fibrillation is shorter. The actual path has been difficult to follow, but there is much probable evidence that the sinuous circus rings are formed about the mouths of the superior vena cava or the *A–V* ostia (Fig. 151). In addition to the irregular sinuous course pursued by the circus ring, similar variable barriers of refractory muscle are interposed in the course of the centrifugal waves. The result is that not only is the fundamental rhythm very irregular, but the times at which various fractions of auricular muscle are stimulated is very variable.

State of Rapid Reëxcitation.—When in any way (*e. g.*, vagal excitation, muscarine, inherent conditions of auricle) the refractory phase is very markedly reduced (0.025 to 0.14 second), the auricle tissue theoretically is able to respond at extremely rapid rates (up to 4300). If, furthermore, we suppose that small circus rings of a few millimeters are formed, it is obvious that extremely rapid rates of excitation might be given to auricular muscle. Such a condition has been found to underly the state of rapid reëxcitation (Lewis and collaborators). From these rapidly completed central circuits, impulses are

sent in all directions by centrifugal waves which, as in clinical fibrillation, do not progress at regular rates or in straight courses to consecutive fractions of auricular tissue. There is this added feature, however: The individual fractions excited are able to respond to these high rates with but feeble mechanical contractions (Rothberger and Winterberg). Consequently, although the auricular tissue is stimulated in a coördinated manner, the incidence of the very feeble fractionate contractions throughout the auricle is not such as to give at any time any definite shortening or elongation of the auricle as a whole.

Summing up the recent experimental work, it may be said:

1. That, in all conditions analyzed, the pace of the auricular excitation—whether regular or irregular—is determined by the time required for the completion of a circus movement, and this, in turn, is actually governed by the length of the central ring and the refractory phase of the muscle.

2. That in none of the conditions analyzed (not even excepting conditions of clinical fibrillation and rapid reëxcitation) is there a lack of coördination in the spread of the excitation wave. The pathway may be impeded at one time and facilitated at another, but there is always a sequential distribution of the centrifugal impulses given off from the central ring to the periphery.

3. The actual presence of a mechanical systole and diastole in conditions of flutter and fibrillations on the one hand, and its reduction or complete absence in rapid excitation on the other, is due to the fact that the minute fractionate contractions and relaxations are or are not summated (*cf.* Fibrillary Waves in Auricular and Venous Pulse).

The Influence of Vagus Stimulation.—It has long been noted that vagus stimulation exerts not only marked but often paradoxical effects on an auricle in the states of flutter or fibrillation. The chief effects that have been reported are shown in the following table:

CHIEF EFFECTS OF VAGAL STIMULATION ON THE AURICLE (AFTER LEWIS, DRURY AND BULGER).

Initial mechanism	Mechanisms under vagal stimulation.	Final mechanisms.
Normal action	Slow normal action → rapid re-excitation → flutter → rapid re-excitation → fibrillation →	normal action continued flutter normal action continued fibrillation
Flutter →	Flutter at advanced rate → rapid re-excitation → flutter → Flutter at advanced rate →	continued flutter normal action
Fibrillation	rapid re-excitation → fibrillation → impure flutter → fibrillation → impure flutter →	continued fibrillation normal action

These contradictory results, which have been much discussed, may be quite logically explained according to the work of Lewis and his associates. It must be recalled that all of these auricular disorders depend upon the existence of a circus ring of larger or smaller circumference, that such rings are only established when an appropriate gap exists between the excitation wave and the refractory tissue, that if, in any way, the gap is closed, circus movements are abolished and the rhythm of the *S–A* node again becomes reëstablished (Fig. 150, *A*).

By reducing the refractory phase of auricular tissue, vagus stimulation may exert quite opposing influences on the length of this gap. When it shortens the gap, the circulating wave takes a more irregular course; if it is reduced to zero, circus movements end; if the gap widens, circus movements become more regular. A few instances may be cited to show how this affects particular types of flutter and fibrillation. In a fluttering auricle a reduction of the refractory phase may either increase the rate of propagation about the circus ring, thereby speeding up the circus movement and increasing the entire auricular rate, or, if the transmission rate is not advanced, the impulse may form shorter circuits, which has the same effect on auricular rate. A condition similar to the latter occurs when a flutter is converted into states of clinical fibrillation or rapid reëxcitation—only in these cases the wave travels around the more minute circuits in much shorter time.

Finally, if in any circuit the rate of impulse transmission increases to such an extent that the gap is closed, all circus movements cease and the auricle resumes its natural rhythm. The actual effects of vagus stimulation are, therefore, so unpredictable, because it is not only impossible to foretell just how great the reduction in the refractory phase will be, nor how this particular reduction will operate in the case of any particular circus ring.

It must be equally clear, on reflection, that certain types of circus movements may exist in which closure of the gap is not favored by a reduction but by a lengthening of the refractory phase. This may explain how either the elimination or reduction of a certain vagus tone (*e. g.*, by atropine or vagus stimulation) may occasionally act to bring either flutter or fibrillation to an abrupt cessation.

The Nature of the Contraction Process in Flutter and Fibrillation.—The nature of the contraction process in the auricle, as a whole, has been difficult to analyze, because each act of ventricular ejection and filling causes passive changes in the length of the auricular tissue, which it is difficult to distinguish from active contraction phenomena. In cases where ventricular systoles were relatively infrequent, however, the author has recently been able to study the "actual contractions" in these conditions.

In flutter that is pure or only slightly impure, each centrifugal

excitation wave is followed after a fairly constant latent period (0.04 to 0.05 second) by a coördinated muscular contraction, differing from normal in its slower gradient, smaller amplitude and shorter duration (*cf.* Fig. 152). Theoretical analysis indicates that, while the smaller amplitude may be satisfactorily accounted for by the slower rate at which individual fractionate contractions are summated and the reduced time that the fractions contract together, the shorter duration cannot be explained unless we assume that the duration of each fractionate contraction is shorter. It would seem that in flutter and allied conditions not only is the refractory phase shorter and the impulse transmitted at slower rates because refractory tissue is interposed, but that the duration of the fractionate contractions is also reduced.

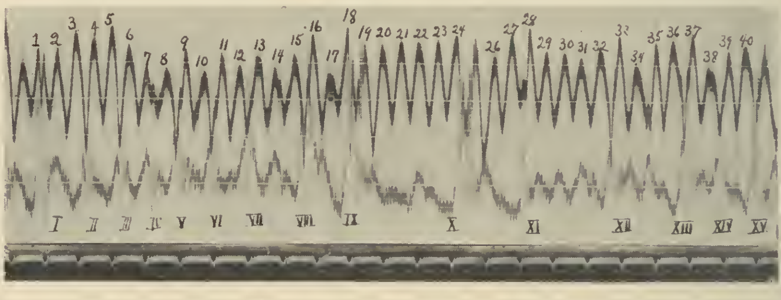


Fig. 152.—Auricular myogram (upper) and heart sounds from interior of right auricle (lower), showing nature of auricular myograms during flutter when ventricular rate is rapid. Auricular rate about 560 per minute. Waves 20–24 and 29–31 are two groups of "pure contraction waves." Other waves modified passively by ventricular action.

In flutter of great impurity, as well as in conditions corresponding to clinical fibrillation, coördinated contractions follow many, but by no means all, of the excitation waves. The contractions which do occur become smaller and smaller as the complexity of the conduction disturbance advances, until, when a rate of excitation exceeding 720 per minute occurs, the auricle, as a whole, does not respond by any coördinated movements (Fig. 153). Theoretical considerations show that the progressive decrease in amplitude as well as the variations in amplitude and duration may be accounted for by the fact that many fractions of auricular tissue remain unexcited and consequently do not take part in the contraction process. The total amplitude of any auricular contraction in fibrillation will, therefore, be determined by the number of fractions that fail to contract and the gradient will be irregular wherever and whenever such fractions fail to be excited. When the irregularity in impulse transmission becomes so irregular that refractory muscle is met at almost every turn (as happens in high rates of excitation) no coördinated contrac-

tions any longer follow the excitation waves. Indeed, the muscle practically becomes a conducting rather than a contracting structure. Inspection of the auricles in such cases shows that the contractions are entirely dissociated and are truly fibrillary in nature.

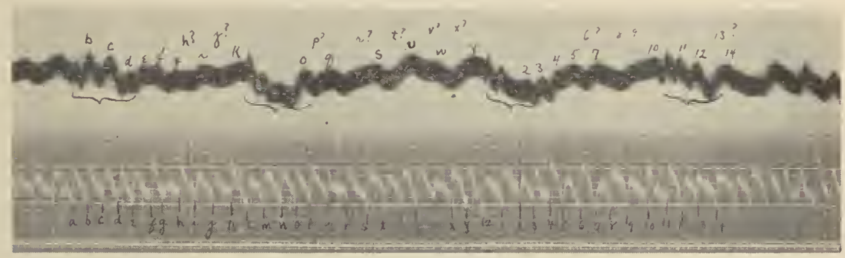


Fig. 153.—Myogram of auricle (upper) and intrinsic electrical deflections (lower) in auricular fibrillation accompanied by $A-V$ block and slow ventricular action. Auricular rate between 600 to 720 per minute. Observe small amplitude and frequent failure of contractions to correspond with electrical deflections. Small letters followed by (?) indicate failure of mechanical response.

Clinical Recognition.—*The Electrocardiogram.*—It is desirable to analyze the typical electrocardiograms derived from clinical cases of fibrillation and flutter, not only because the conditions can thus be determined with great certainty, but also because they give us the clue to many simple signs that may be used in diagnosing the conditions without recourse to graphic registration.

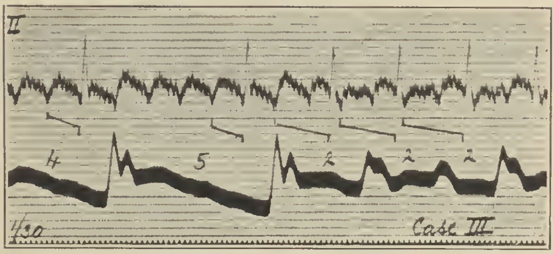


Fig. 154.—Radial curves and electrocardiogram in auricular flutter, showing how the *As–Vs* interval varies when the ventricle responds irregularly. Figures indicate the scheme of regular irregularity present. (After Lewis.)

In pure auricular flutter the electrocardiogram shows a continuous series of small P waves recurring at rates ranging from 230 to 350 per minute (Fig. 154). They are characterized not only by their constancy in form, but also in their remarkable regularity, the variations in different cycles ranging on careful measurement from 0.9 to 7.7 σ (Lewis and associates). Their contour varies in different cases, but they never resemble normal P waves. Usually, the upstroke is abrupt, the summit blunt and the downstroke more gradual (Fig.

154). The wave may be notched either on the upstroke or downstroke. Interspersed between the groups of P waves (*e. g.*, after every second, fourth or fifth) are ventricular complexes. In some cases the ventricular complexes occur at irregular intervals (Fig. 154). It is clear that the ventricular rhythm may be quite regular or somewhat irregular, the rate per minute being either rapid, normal or somewhat slower, depending upon the degree of block. Very rarely the condition is complicated by complete block, in which case the ventricular beat is naturally very slow.

As such records correspond closely to limb leads taken from experimental animals in a state of true flutter, we can only conclude that parallel conditions exist. Undoubtedly, *clinical flutter* is also a condition where the rapid auricular rate is induced by circus rings of excitation found about the great veins. It is obvious, however, that the auricular rates are somewhat slower in man than in animals, which can readily be interpreted as due to the larger paths formed in the larger human heart. Lewis has calculated that an auricular flutter with a rate of 240 corresponds approximately to a circus ring 125 mm. in circumference, whereas a rate of 350 indicates a circumference of about 85 mm.

Limb leads taken from *clinical cases of auricular fibrillation* are characterized by the absence of waves that resemble P waves. Usually, they are replaced by oscillations of varying rate and form, upon which minute quivers are often superimposed; or the line may almost be straight, showing only very fine oscillations. Many records, however, show occasional or periodic intervals, where distinct waves more or less suggestive of P deflections occur. In some records they are always present (Fig. 155). These waves differ from those in flutter in that they are irregular in *form, amplitude and spacing.* At irregular intervals, ventricular complexes occur without reference to the larger auricular deflections, if these are present. It is obvious that the ventricular rate is very rapid and irregular.

By taking chest leads, however, which are in a more favorable plane with the circus rings, large auricular deflections, not unlike those found in limb leads of auricular flutter, recur about 470 to 500 times per minute even in cases where no vibrations are found in limb leads. It is too early to foretell whether such waves will be found without exception in all cases of fibrillation. Nevertheless, such records clearly favor the view that clinical fibrillation, like the condition analyzed in animals, is due to a single excitation wave traveling at irregular rates through a small sinuous circus ring not more than 66 mm. in circumference (Lewis). The centrifugal excitation waves given off from this mother ring not only excite the various fractions of auricular tissue at irregular rates, but many at least pass the $A-V$ node and induce a ventricular systole. The ventricular rate, however, is never as rapid as the circus movement, for many impulses never reach the ventricular tissue, owing to blocks.

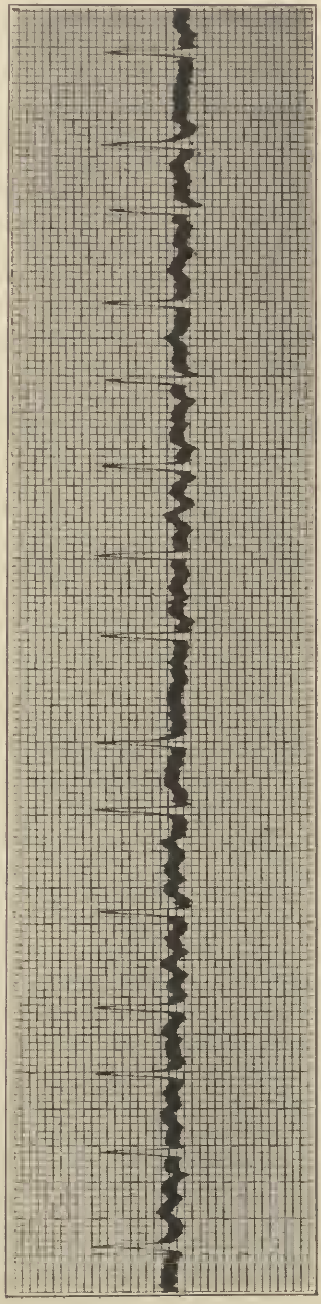


FIG. 155.—Electrocardiogram in a case of auricular fibrillation. (Courtesy of Dr. H. B. Williams.)

While the electrocardiograms offer a certain means of distinguishing between states of pure flutter (in which the rate of excitation about the central ring is regular) and state of fibrillation (in which the spread of excitation is irregular both in the central ring and its offshoot paths), the recognition of so-called "impure flutter" (in which the central ring is regular, but where blocks occur in the centrifugal paths propagation alone) is, as yet, not so certainly established. Heretofore, it has been customary to so classify all cases in which waves irregular in size, form and spacing recur in limb leads (Fig. 155). The facts that similar oscillations are derived from cases clearly demonstrated to be fibrillations by chest leads (Drury and Iliescu), and that such oscillations often appear and disappear in continuous records, make it doubtful whether impure flutter in its "stricter" meaning can be thus interpreted. Perhaps it will be found possible, by the study of clinical cases, to demonstrate the condition of impure flutter by showing that, while the amplitude and spacing of individual waves are irregular, this irregularity can be reduced to some regular scheme. This we might expect in cases where the regularity of the circus rhythm compensates for conduction irregularity in the centrifugal paths. Until further investigative work has been done, however, it is doubtful whether such a refinement in diagnosis should be undertaken. The important fact to bear in mind at present is that it is very precarious to diagnose transitions from impure flutter to fibrillation and, *vice versa*, on the basis of appearance and disappearance of irregular large waves in the limb leads.

The Arterial Pulse.—In the previous analysis it was pointed out that while the ventricular rate is frequently rapid in flutter, it may be quite normal or even slow. Since the ventricular response always occurs in definite relation to an auricular contraction, we may expect that the rhythm of the pulse beats is either regular or so spaced that a compensated rhythm occurs. Thus, as shown in Fig. 154, two auricular beats occur for the single pulse wave labeled 2, four in the wave so labeled, etc. Consequently, it has been suggested that the condition may be diagnosed by careful measurements of pulse beats (Lewis). No one can gainsay that such records can be clearly interpreted when the auricular condition is known. That a diagnosis can often be made from arterial tracings alone is doubtful. No one could foretell, for example, from a regular radial pulse of 150 per minute, at what rate the auricles are beating. The only favorable cases are those in which irregular blocks exist, but these also are not always simply interpreted. Frequently a pulsus alternans exists which is confusing. Again, the amplitude of the waves is influenced by the variation in the preceding pauses, hence the pulse beats following a 2:1 block are weak and may simulate premature systoles. Lastly, the block is accompanied by variable *As–Vs* pulse intervals,

isometric periods and pulse transmission times, which tend to disturb any exact measurements which should theoretically obtain. Thus, in Fig. 154 the three arterial waves labeled 2 are all of a 2:1 rhythm, as shown by accompanying electrocardiograms, yet the length becomes progressively shorter in consecutive waves.

Fibrillation, on the other hand, can usually be diagnosed from a careful study of the arterial pulse alone. The rate may be fast or slow, although a rapid rate is more frequent if digitalis has not been used. The characteristic feature is the absolute irregularity of beats. No sequence can be discovered in the irregularity. Beats of different size follow each other in varied order, and it has often been pointed out that, contrary to other conditions, there is apparently no relation between the strength of the pulse beat and the preceding pause. From this, the inference is sometimes drawn that the ventricle does not obey the law that the strength of contraction is inversely related to the preceding period of rest. The writer has shown, however, that this law is apparently not always obeyed in normal pulses, partly because the size of the pulse amplitude is also determined by the varying diastolic pressure existing at the time of the ejection. A similar explanation has recently been given to the variable amplitude of the pulse waves found in auricular fibrillation (Einthoven and Korteweg).

Since there is still some doubt whether all such types of completely irregular pulse are due to auricular fibrillation (Hoffmann), it is desirable to check the diagnosis in other ways.

The Venous Pulse.—The venous pulse is considered of great value in diagnosing and differentiating auricular flutter and fibrillation; indeed, the discovery of flutter is due to the use of venous pulse tracings (Hertz and Goodhart, Jolly and Ritchie). Chief stress has been laid upon the regular recurrence of *a* waves in flutter, especially when the ventricle does not respond too frequently (Fig. 79, *F*). In such cases, it is possible, by estimating the waves during ventricular beats, to actually determine the auricular rate. When, however, the ventricular response is frequent (*e. g.*, 2:1 block) and the duration of diastoles is very short, the *a* waves readily become fused with *c* and *v* waves.

Even when *a* waves are clearly indicated, a certain amount of care must be exercised in view of our stricter definition of flutter. As analyzed later, large recurring diastolic waves are frequently found in cases of frank fibrillation. The chief value lies in their regularity, but in regard to this point, it must also be recognized that the regular waves often found in polygrams may owe their regularity to an inherent lever movement rather than a venous vibration. Such an instance of doubtful flutter is shown in an optical tracing of Fig. 156, for while oscillations occur at a rate of 300 per minute no complete regularity exists. In polygram records this was not apparent.

According to the description given by Mackenzie and Lewis, venous polygrams in auricular fibrillation are characterized: (*a*) By the absence of *a* waves; (*b*) by the presence of prominent systolic waves, rising rapidly to a summit and often showing a notch or dip in mid-systole (Fig. 79, *h*). This "ventricular type of venous pulse" has often been regarded as diagnostic of tricuspid regurgitation. A study of optical tracings indicates that this is not correct. Thus, six types of systolic waves with distinctive contours and time relations may be distinguished (Niles and Wiggers): (1) An intensified impact wave, the most common and often the only characteristic feature, indicating vigorous ventricular action; (2) a peaked impact followed by a rapid systolic drop, due to light pressure of the tambour; (3) the

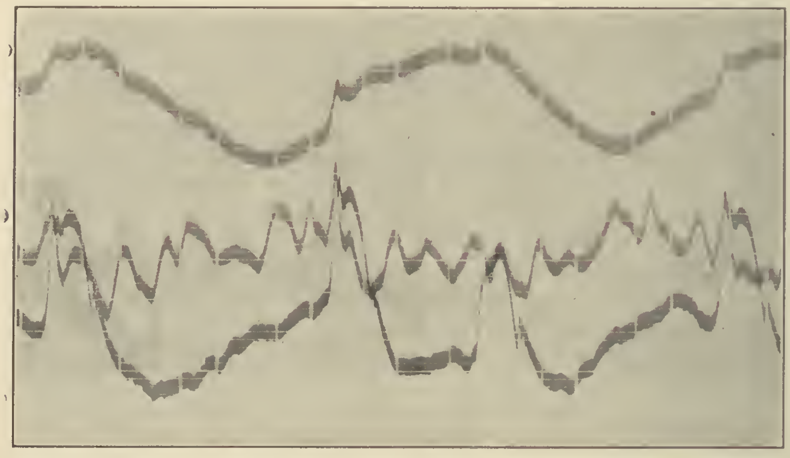


Fig. 156.—Optical tracings from case of impure auricular flutter. Respiration (upper), supraclavicular venous pulse (middle) and subclavian pulse (lower). Variations in contour of so-called *a* waves very variable. S^1, first sound due to ineffective systole.

intra-auricular type of systolic variation, so-called from its resemblance to intra-auricular pressure curves found in animals, occurring in clinical cases only when ventricular systole is weak; (4) double systolic waves, attributed to a systolic tug of the ventricle on the auricle and large veins; (5) a systolic impact followed by a stasis wave, present when intravenous pressure is high; (6) a regurgitation wave, composed of a steep rise continued into a systolic plateau with murmur vibrations superimposed. These types are illustrated in Fig. 157.

This study showed: (1) That tricuspid regurgitation, as indicated by the presence of true regurgitation waves, is a rare accompaniment of auricular fibrillation; (2) that the contrary opinion, arrived at by the frequent presence in polygraph tracings of ventricular types of waves, is due to the fact that the contour of intensified impact

waves is distorted by polygraph levers, so that they simulate regurgitation waves.[1]

When the diastolic pauses are of some length, small movements recurring 350 to 500 times per minute are frequently found. They are irregular in time and size and are generally attributed to fibrillary movements (*cf.* Fig. 78, *II*). Occasionally, numerous diastolic waves of larger amplitude recur either in groups or in consecutive cycles. They have sometimes been considered as diagnostic of coarser states of auricular contraction (Hewlett and Wilson). Experimental work indicates, however, that the size or number of these waves is not directly associated with the extent or incidence of auricular con-

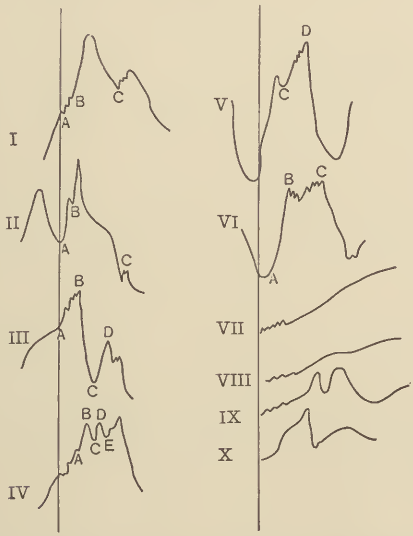


Fig. 157.—Series of transcribed systolic waves occurring during auricular fibrillation (*I–VI*). Typical diastolic waves found in auricular fibrillation (*VI–X*). *I*, *II* normal and intensified impact waves; *III*, intra-auricular type; *IV*, *V*, systolic impact plus stasis wave; *VI*, regurgitation wave.

tractions (Wiggers and Niles). Fine fibrillating movements of the auricle do not in themselves produce waves in the jugular. They produce neither pressure variations in the auricle nor exert any traction upon the veins. The only factor capable of producing jugular

[1] Lewis, in his last book, dissents from the view that any of these waves are arterial impacts, on the ground that they can be directly observed in the smaller veins and recorded by projecting the shadow of such a vein on a recording surface. Aside from the dubious value of such records (*cf.* page 221), it may be added that the authors did not imply that a direct carotid impact was necessarily the cause of these waves. Indeed, we have good reason to believe that an impact of the aorta on the distending right auricle often occurs and that the wave thus produced is transmitted up the veins. Such instances are shown in Fig. 157, lower curves *III* and *IV*. This does not in any way invalidate our conclusions as to the significance of these waves.

waves during fine fibrillation seems to be the traction exerted by the position changes of the ventricle on the auricle and large veins. This may, in a measure, explain why the diastolic waves recorded from the apex and second left interspace of patients often closely correspond with those simultaneously recorded from the jugular. When their etiology is considered, the term "fibrillary waves," commonly applied to the smaller of these variations, is poorly chosen. The coarser contractions of the auricle during impure flutter also produce no appreciable pressure changes within the auricle. At times they are vigorous enough, however, to exert a traction upon the venous walls. Hence, the diastolic waves during impure flutter may be regarded as partly of ventricular and partly of auricular origin, or, as is frequently the case, as due to an interference of the two.

Clinical Signs and Symptoms.—The symptoms of *auricular flutter* resemble those of fibrillation, but are of no diagnostic significance. Palpation of the radial pulse is of no assistance in diagnosis. Rarely the rapid auricular beats give rise to sounds which can be heard on auscultation (Cohn).

The onset of auricular fibrillation may proceed unannounced or, at least, may not give rise to symptoms which attract the attention of the patient. Occasionally, however, acute symptoms suggesting circulatory failure or decompensation occur, *e. g.*, breathlessness, dyspnea, dizziness or even syncope. Some patients experience thumping or surging sensations in the chest and neck; others are conscious of their irregular ventricular mechanism. In general, the symptoms depend upon how well the arterial circulation is maintained. The symptom which most frequently directs attention to the condition is the patient's recognition that his range of accommodation is reduced (Mackenzie).

Auricular fibrillation is readily recognized by palpation of the pulse. The pulse beats are entirely irregular in rhythm and force (pulsus irregularis perpetuus (Hering)). The rate is usually rapid unless patients have taken digitalis. Contrary to other types of irregularity, it is not affected by exercise. The condition can also be recognized by auscultation, the heart sounds following each other in complete disorder. They vary in intensity from beat to beat and occasionally a second sound is lacking. These constitute the ineffective systoles which cause no ejections and, consequently, no pulse. When, therefore, the rates of the ventricular sounds and arterial pulse are compared they show a discrepancy in favor of the sounds. This has been termed the "pulse deficit" (Draper). Coincident murmurs add to the confusion in auscultation. When fibrillation supervenes upon a mitral stenosis the presystolic murmurs disappear, but the early diastolic murmur during ventricular filling persists or is accentuated. Systolic mitral or aortic murmurs continue to accompany each systole, except when the rate is very rapid. Systolic and diastolic blood-

pressures vary from beat to beat, so that it is impossible to measure them by clinical methods. (For details, see page 365.)

Prognosis.—Even before the cause of the irregular pulse had been recognized, it was regarded as of grave significance. This statistical fact, no doubt, is due to the frequent association with mitral lesions—an association so common that it has been termed the "mitral pulse." Soon after the recognition of auricular fibrillation, pathological studies showed that extensive degenerative changes exist throughout the heart (Koch, Mackenzie, Schönberg, Cohn, etc.). On this basis fibrillation came to be regarded by many as a sign of general myocardial involvement (Mackenzie).[1]

Recently, however, facts have accumulated which give a more cheerful aspect. Transient attacks, lasting hours, days or weeks, have been frequently observed in acute infectious and febrile conditions (pneumonia, influenza). Further, long-standing attacks have been resolved by the use of quinidine. Recent experimental work, moreover, has shown that the fibrillating process is not determined by degenerated muscle but depends entirely upon functional attributes of auricular tissue. This has necessitated a change in view as to its pathogenesis which can no longer rest upon damage to muscle (Cohn). The prognosis is, therefore, determined more by attendant conditions than by fibrillation *per se.* Superimposed on valvular lesions or myocardial weakness it is unfavorable, although even such individuals have been known to lead useful and energetic lives for ten to fifteen years.

The immediate prognosis depends upon how efficiently the heart is able to maintain the circulation under the strain of an irregular rhythm. The extent of the pulse deficit is of immense importance, for the efficiency of the circulation is largely determined by the number of effective systoles. The measurements of the highest and lowest systolic pressures or of the average systolic pressure is, therefore, capable of giving evidence as to the prognosis.

The prognosis in flutter is commonly regarded as more favorable. The fact that such a condition may be converted into fibrillation by the use of digitalis after which the heart regains its normal rhythm has contributed to this general idea. Investigation showing that essentially similar mechanisms are involved in both flutter and fibrillation, and that fibrillation may also be terminated in many cases by the use of quinidine, make it doubtful whether the life expectancy in fibrillation is really less than in flutter.

VI. VENTRICULAR FIBRILLATION.

Clinical Physiology.—Fibrillation of the ventricle is a familiar event to the experimental investigator, and its gross characteristics have

[1] For tables showing the relation of auricular fibrillation to age, sex and diseases, *cf.* Semerau (Ergebnisse der innere Med., 1921, **19**, 134).

been frequently described. It always results after the application of a strong tetanizing current to the ventricles and occasionally is a result of single shocks (de Boer). It is the mode of death when relatively low-voltage currents are passed through the body in electrocution (Cluzet and Bonnamour).[1] Thermal (Schlomovitz), mechanical and chemical irritants frequently induce the condition, as do toxic doses of many drugs (Cushny, Lewis) (*cf.* also page 38).

When fibrillation is induced in any of these ways the heart passes progressively through three stages, but these are not sharply demarcated. The onset consists of premature systoles repeated with increasing frequency, so that finally groups are formed. In electrocardiograms they are recognized as aberrant ventricular complexes. This gradually or rapidly dissolves into a second stage of ventricular tachyrhythmia which dominates both auricles and ventricles. Again, large aberrant waves characteristic of ventricular tachycardia are seen. They rapidly change into waves of a broader type, however, and at this time the ventricles give the appearance of having undulatory waves of contraction sweeping over them, a condition that is well designated by the German phrase "Wogen und Wühlen." The ventricles contract so rapidly that complete relaxation is impossible and, consequently, they appear to remain contracted. Finally, these also disappear and only minute localized twitchings appear over the entire ventricle, which now feels as a wriggling mass of tissue. This represents the true stage of fibrillation. From this condition large hearts rarely recover, but in smaller animals (*e. g.*, cats) such recovery may take place. As Garrey has pointed out, recovery is conditioned largely by the mass of fibrillating tissue.

While the fundamental nature of the ventricular fibrillation has been the cause of considerable work, its true nature has not yet been definitely established. Its similarity to auricular fibrillation, the facts that it develops through stages of premature contraction, that tachyrhythmia similar to flutter takes place, that it may be elicited by single stimuli given at the very end of a refractory phase (de Boer), that it may be abolished in small fragments of tissue separated from the rest of the ventricle (Garrey), all point to a depression of conduction rate, and reduction in refractory period leading to the formation of circus rings as in auricular fibrillation (*cf.* MacWilliam, Porter, Mines, Gewvin, de Boer, Garrey) (*cf.* also literature under Auricular Fibrillation).

Clinical Recognition.—As ventricular fibrillation leads speedily to death, its clinical recognition, by means of the electrocardiogram, is almost entirely a matter of chance. A number of such cases have been reported, however (Halsey, Hoffmann, Rohmer, Robinson). Records from these cases show that the essential mechanism cor-

[1] *Cf.* also Gildemeister and Diegler (Ztschr. f. d. ges. Med., 1922, **28**, 144).

responds to the stages above enumerated in experimental fibrillation. Robinson and Bredeck, and more recently Dieuaide and Davidson, have instanced cases where recovery temporarily occurred in patients verging on complete fibrillation.

DISTURBANCES IN IMPULSE CONDUCTION.

VII. HEART-BLOCK.

Clinical Physiology.—Views are still conflicting as to whether impulses originating in the *S–A* node reach the *A–V* node by way of auricular muscle tissue (Lewis) or whether they pass over functionally specialized

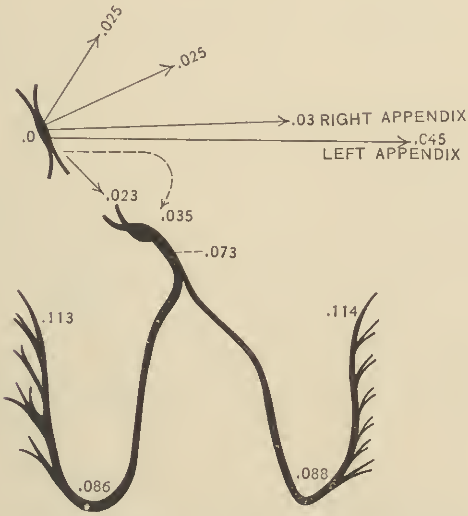


Fig. 158.—Diagram showing approximate time of spread of impulse from *S–A* node to different portions of the auricle and over His-Tawara system.

pathways (Eyster and Meek) (*cf.* page 31). The preponderance of evidence indicates that while no single, well-defined pathway serves to conduct impulses between these nodes to the exclusion of all others, impulses spread preferentially by a definite pathway of auricular muscle between these nodes. Arriving at the *A–V* node, impulses are delayed briefly and then speed to the branches and arborizations of the His-Tawara system to stimulate ventricular muscle. The order and approximate spread are diagrammatically shown in Fig. 158.

It is obvious that the passage of impulses may be delayed or blocked in several locations, viz.: (*a*) In pathways between the *S–A* node and auricle; (*b*) between the *S–A* node and ventricle; (*c*) at the *A–V*

node or His bundle; (*d*) in the bundle branches; (*e*) in the arborizations or their ventricular junctions. Before entering into a discussion of the separate types, it is desirable to discuss the physiological nature of the block and the known means for its experimental production. This may be most satisfactorily done by anticipating the effect of experimentally produced block in the *A–V* bundle.

Experimentally, *A–V* heart-block may be produced most advantageously by cutting or compressing the different portions of the His-Tawara system. Such experiments have proven very instructive. Complete transection or ligation of the His bundle causes cessation of all impulse transmission to the ventricle (Humblet, Hering, Erlanger, Cohn and Trendelenburg). When this occurs, the ventricle temporarily stops and after a short interval, reassumes an independent idioventricular rhythm. This is termed complete heart-block. If the bundle is only partially divided or slightly compressed, various stages of partial block may be produced. The consecutive events may be summarized as follows:

1. A delayed conduction resulting in an increase in the *As–Vs* and *P–R* intervals.

2. An occasional failure of the ventricle to respond to stimuli when the auricle does so.

3. A regular dropping of ventricular beats, so that the ratio of auricular to ventricular beats may be as 10 : 9, 8 : 7 or 4 : 3.

4. A regular ventricular response to every second, third or fourth sinus impulse, as indicated by the fact that such ratios as 2 : 1, 3 : 1 or 4 : 1 are established between auricular and ventricular beats.

5. An entire failure of impulses to reach the ventricle, as shown by the fact that the ventricular rhythm bears no relation to the auricular.

The last three instances are rendered clearer by the aid of Fig. 159. In other words, it is possible to produce three types of disturbances, viz.: (*a*) Incomplete block, or delayed conduction; (*b*) partial block; (*c*) complete block.

Why conduction fails entirely in complete block is readily understandable; why, however, occasional impulses pass freely and others not at all in partial block must be explained. Several interpretations suggest themselves: It is conceivable that in partial block the irritability of the *A–V* tissue is so reduced that the intensity of the natural impulse remains subminimal and a single excitation, therefore, cannot evoke a reaction expressing itself by conduction of an impulse. A simple experiment in elementary physiology teaches, however, that a muscle excited by a series of such subminimal stimuli may thereby have its irritability so increased that it finally reacts. In similar ways we may suppose that in the case of 3 : 1 block, for example, two subminimal stimuli bombard the *A–V* node and bundle and have no other effect than to increase its irritability, while the

third impulse actually initiates a conduction wave. In this explanation it is further necessary to assume that, with the passage of conduction process, the irritability is once more depressed and requires restoration by the tonic effect of two further subminimal stimuli before it is again able to conduct. According to a more recent and, in some respects, a more satisfactory hypothesis, the condition is associated with a further prolongation of an already long refractory phase of junctional tissue.[1] According to this view, it will be necessary to assume in the case of 3 : 1 block that two impulses arrive during the refractory phase while the third strikes a partially blocked

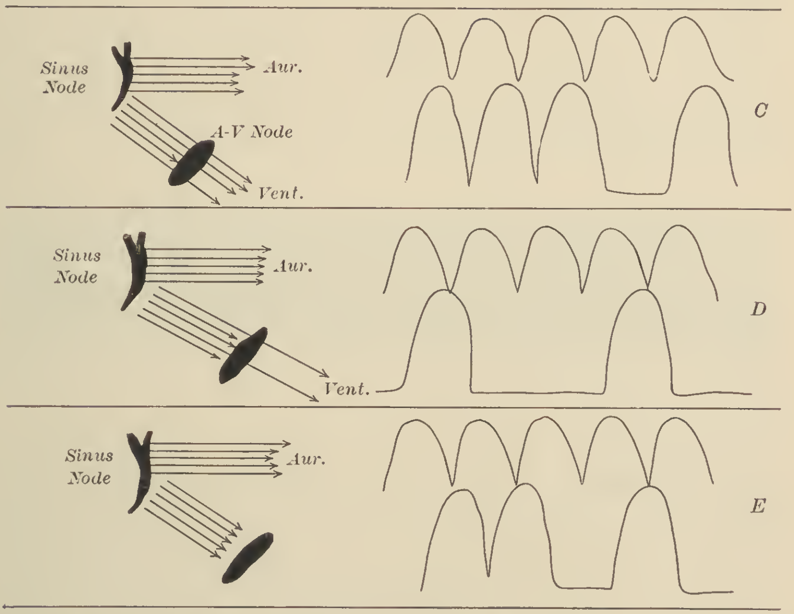


Fig. 159.—Diagram illustrating the nature and cause of 4 : 3, 3 : 1 rhythm and absolute sino-ventricular block. (The diagram of complete block, *E*, is wrong to the extent that the ventricular beats should have been regularly spaced.)

tissue during a responsive period and so permits a reaction (Lewis). Finally, it is possible that all impulses actually pass the *A–V* node and bundle, but that their strength is so reduced that they remain subminimal until the irritability of the ventricle itself is raised by a sufficient period of rest (Erlanger).

Sino-auricular Block.—Clinical Physiology.—By gradual isolation of the *S–A* node through incision or ligation, Eyster and Meek have shown, by recording simultaneously the activity of the *S–A* node,

[1] *Cf.* page 36.

A–V node and auricle that both a partial and complete sino-auricular block may be produced. In partial block, the impulses are regularly initiated in the S–A node, but a 2 : 1 or 3 : 2 block may develop, in which both auricular and ventricular contractions drop out. In complete block, the impulses initiated in the S–A node are not permitted to leave it, consequently an atrioventricular nodal rhythm develops. More recently, evidence has been adduced (Eyster and Meek) which indicates that the preferential sinoventricular pathway may be alone affected experimentally, producing a condition in which every sinus impulse is transmitted to the auricle, but only every other beat is conducted to the ventricle. It may, therefore, be desirable to differentiate between sino-auricular block, in which impulses are blocked in both auricle and ventricle, and sino-ventricular block, in which the ventricular pathway alone is affected. Experimentally, such a sino-auricular block is extremely rare, owing to the diffuse nature of the conducting pathways between the S–A and A–V nodes (Eyster and Meek).

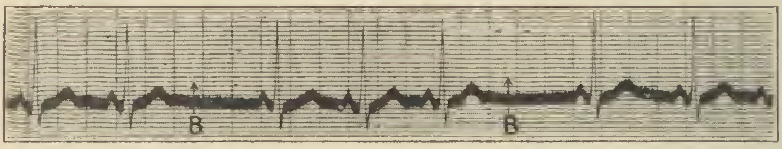


FIG. 160.—Electrocardiogram, Lead II, from a case of sino-auriculo heart-block. Approximately at B, a complete complex is dropped out. (Courtesy of Dr. Harold Feil.)

Clinical Recognition.—In the simplest forms of sino-auricular block, one or several complete auricular and ventricular contractions occasionally or periodically drop out; in other words, an otherwise regular rhythm is interrupted by a long cycle. The rhythm is, however, a compensated one, *i. e.*, the long cycle is then equivalent to two normal cycles. Consequently, the condition may be suspected when graphic records, such as the venous pulse and electrocardiogram (Fig. 160), show waves of normal contour and sequence which abruptly fail and in which the intervals of the long beats approximately equal two normal beats.[1] The latter criterion is supposed to differentiate the condition from phasic sinus irregularity, while the normal relation of a–c waves in the venous pulse and the P–R waves in the electrocardiogram differentiate it from compensated ventricular extrasystoles.

Sinoventricular block is generally supposed to be a rare affection and associated either with structural or functional defects in auricular conduction. These conclusions were reached because it has

[1] It is, of course, impossible by known methods to obtain direct evidence of continued activity in the S–A node during dropped beats, and since these beats may possibly be due to other causes (*e. g.*, failure of sinus rhythm or failure of muscle to respond) their diagnosis is based on presumptive rather than quite certain evidence.

frequently been found associated either with the toxic action of drugs or in myocardial affections. Thus, it has been observed frequently after the use of digitalis (Cushny, Levine, Parkinson, White), aconite (Cushny) and morphine (Cohn and Eyster and Meek). It has also been found in acute infections, for example in influenza (Mackenzie, Cockayne), acute arthritis (Brown) and diphtheria (Smith). More recent observations, however, question both the rarity of the condition and its pathological significance. It appears to occur frequently in perfectly healthy individuals, where it may be abolished by exercise, by swallowing, by use of atropine or mental excitement, and may be induced or rendered more pronounced by vagus pressure (Eyster and Evans, Gallavardin and Dumas, Robinson and Draper, Stokes, Smith).

Complete sino-auricular block is difficult to diagnose, owing to the fact that an atrioventricular rhythm develops and no evidence of a rhythmic functioning of the *S–A* node is obtainable. As Eyster and Meek point out, however, *S–A* block must be regarded as a potential possibility in all cases of *A–V* rhythm.

Atrioventricular Block.—By atrioventricular block is meant a condition where impulses are delayed, partially or completely blocked either in the *A–V* node or the His bundle. It may be experimentally produced in a variety of ways, and we have evidence that similar processes operate in those experiments which Nature chooses to perform on man. The chief experimental causes may be tabulated as follows:

(*a*) Mechanical pressure of varying degrees applied by means of a clamp or ligature.

(*b*) Vascular impairment produced by ligation or artificial embolism of the coronary vessels.

(*c*) Applications of cold.

(*d*) Chemical agents, *e. g.*, asphyxiation, anoxemia.

(*e*) Drug action, *e. g.*, epinephrin, digitalis.

(*f*) Certain toxins, *e. g.*, diphtheria.

(*g*) Vagal stimulation, particularly the left.

(*h*) Tissue destruction, as by cutting, ligation or injection of destructive chemicals.

Clinical Physiology.—The fundamental nature of incomplete, partial and complete block has already been discussed (*cf.* page 492). As long as block is partial, the impulses originate in the *S–A* node, and while the number of auricular beats exceeds those of the ventricle, the latter are always preceded by an auricular contraction. In complete heart-block, a slow but regular idioventricular rhythm is established in the common bundle, below the point of injury. Ventricle and auricle then beat without relation to one another.

Clinical Recognition.—(*a*) *Partial A–V Block.*—Partial heart-block may be accompanied by no subjective symptoms other than the

existence of a slow pulse or the sensation of an occasional intermission. If the slowing is great, however, it may be accompanied by attacks of syncope similar to those described in complete block.

A scheme for determining the existence of minor degrees of block from the arterial pulse tracings alone was devised by Wenckebach, who diagnosed conduction disturbances, for example, in those forms of intermitting pulses in which the first wave after an intermission is longest, the next shorter and the last one before another intermission, longer again. Wenckebach contended that the conduction from auricle to ventricle is progressively decreased during activity, so that the ventricle follows the auricle with a progressively longer interval until, finally, the passage of the impulse fails altogether, causing a pulse intermission. The long rest thus resulting increases the conductivity again and allows a more rapid impulse conduction to follow.

In such an analysis no account is taken of the varying transmission time of the pulse, which may readily account for the slight variation present. Furthermore, it has been shown that such a periodic reduction in conductivity does not necessarily occur. It is, therefore, questionable whether disturbances in conduction can be safely determined from the arterial pulse tracings alone.

Either one or two things characterize the venous pulse (Fig. 78, *E*) in this condition, viz.: (*a*) A prolongation of the *a–c* interval, and (*b*) the presence of *a* waves followed neither by *c–v* groups nor arterial waves. The variation in the *a–c* interval may be the only evidence of a disturbed conduction. When this interval becomes longer than 0.3 second, such a disturbance may safely be assumed; occasionally, it may equal 0.6 to 0.7 second. The *a–c* interval may lengthen from beat to beat until an intermission occurs. In many cases, however, no lengthening of this interval is found. When *a* waves occur in their regular sequence and are not followed by a *c–v* group and an arterial pulse intermission, a periodic block is very likely present. The intermissions may recur at long or at short intervals, regularly or irregularly. If the arterial wave fails regularly, so that two, three or four *a* waves occur to every arterial wave, the condition is evidently a 3:1 or a 4:1 block (Fig. 78, *E*). The electrocardiograms show normal *P* waves recurring in regular sequence (Fig. 161). These are followed, *except when the ventricle fails to contract,* by regular *R–S–T* complexes. The *P–R* intervals may not vary or they may increase in length to 0.3 second (normal 0.13 to 0.18).

(*b*) *Complete A–V Block.*—Complete heart-block gives rise to certain symptoms and signs that make one at once suspicious of the condition. These are: A slow regular pulse (30 to 40 per minute) and signs of dyspnea and weakness on exertion. If these are accompanied by syncopal attacks, muscular twitchings and epileptic seizures

(in short, the characteristic Stokes-Adams syndrome) the diagnosis is quite certain. Attention has already been called to the fact that the Stokes-Adams syndrome may occur from any cause producing cerebral anemia, and that these symptoms should not be regarded as necessarily associated with block. These attacks occur during two stages of the disease: (*a*) When block becomes complete and the ventricles stop entirely before inaugurating their independent rhythm; (*b*) after its establishment, when the ventricular rate is too slow to maintain an adequate cerebral supply. The condition may be definitely recognized by combined arterial and jugular tracings or by the electrocardiogram. The jugular pulse shows a regular sequence of *a* waves and a haphazard sequence of waves due to ventricular systole. The arterial pulse is always slow and usually regular (Fig. 78, *G*).

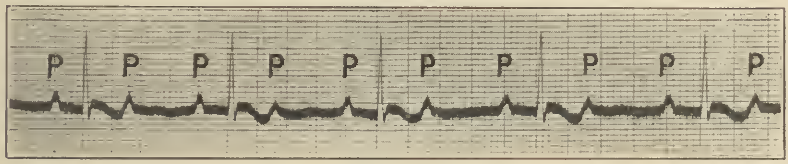


Fig. 161.—Electrocardiogram, Lead II, of a case of 2 : 1 *A*–*V* heart-block. Observe that the regularly spaced *P* waves are twice as numerous as ventricular complexes. (Courtesy of Dr. Roy Scott.)

The electrocardiogram (Fig. 162) shows, at regularly spaced intervals, distinct *P* waves which may be unusually large. Most of them are isolated, but here and there, evidently without relation to the *P* waves, groups due to ventricular contraction appear. In most cases these are of typical normal type. Occasionally, the typical form of the ventricular complex undergoes minor changes. Thus, R_{II} may be relatively low and S_{II} deep. Another variation consists in a broadening of the *R* wave, which may stretch over an interval of 0.15 second (normal 0.04). All of these variations may still be regarded as showing that the block occurs above the division of the *A*–*V* bundle and that the new rhythm originates in the *A*–*V* system.

In other cases the ventricular complex resembles curves such as have been obtained on severing the right or left bundle (Fig. 163), and from analogous animal experiments it has been assumed that the conduction disturbance extends to the branches as well.

Causation and Prognosis of Clinical Heart-block.—It has been established, by careful histological postmortem study of cases, that heart-block is frequently associated with definite lesions of the *A*–*V* node, the His bundle or its branches.[1] It is important to observe that no

[1] A tabular summary of 63 cases studied before death and postmortem is given by Bachmann (Jour. Exp. Med., 1912, **16**, 25).

instance of complete destruction of the bundle has been found in authentic reports without the presence of heart-block during life.

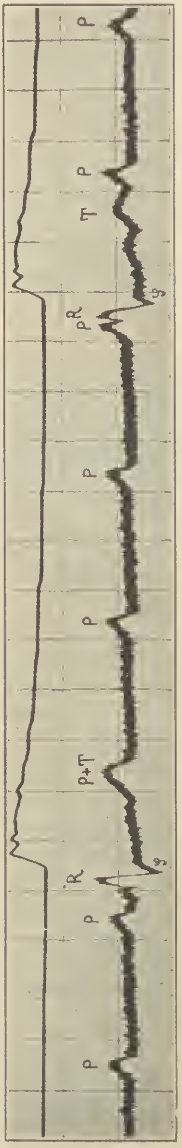


Fig. 162.—Radial pulse and electrocardiogram in total heart-block. (After Pribram and Kahn.)

Inflammatory reactions with edema, cellular infiltrations—such as occur during rheumatic fever, influenza, typhoid, pneumonia and syphilis, septic foci, postinflammatory fibrosis, fatty and calcareous

degenerations, ulcerations, tumors and, by far the most frequent, gummata—have all been found in cases that succumbed to this condition (for reference, see Lewis). When such lesions involve the bundle, they are not, as a rule, confined to it but are distributed throughout the myocardium.

Compression block may, however, occur without destruction of tissue. Thus, an increase of fluid within the sheath and bursa surrounding the conducting bundle, as well as pressure exerted by tumors, aneurysm (Friedlander and Isaacs), etc., may be the cause of block. Twelve cases of congenital block caused by a defective development of the *A–V* bundle have been reported (*cf.* White, Eustis, Kerr, Carter and Howland). While some of these cases have been recognized as early as the seventh day, others apparently remained undetected until twenty years of age. Heart-block is frequently found, however, in cases which show no lesion on postmortem examination. It must be supposed that in such cases a toxic action has modified the conductivity before it has had a chance to produce a pathological change. Among the toxins which act in this way are those of acute infections. This is probably a frequent cause of heart-block in children (Eyster and Middleton). Diphtheria produces an especially acute and fulminating type of block (Smith). Heart-block may follow the therapeutic use of drugs, *e. g.*, digitalis (Cohn, White and Sattler) and salicylates (Sicard and Meara). Heart-block of a transient nature may be due to excessive vagus influence and, in predisposed cases, may indeed be induced by vagus compression (von Hösslin, Mackenzie, Robinson and Draper).

The prognosis must be considered from two angles: (1) The amount of damage that probably exists in the heart, and (2) the ability of the altered heart rate to maintain an efficient circulation.

If the heart-block is complete and there is evidence of involvement of the branches as well, it may safely be assumed that extensive degeneration of the heart has taken place and the possibility that the patient's life may terminate at any time must be borne in mind. Mackenzie, however, states that some cases may lead a quiet life for ten to fifteen years before death occurs. If the block is incomplete, it is not necessarily an indication of structural impairment of the heart, and the prognosis is more favorable unless the degree of block increases.

The question of immediate importance is whether the beat of the heart during block is capable of maintaining an efficient circulation. A certain minimal rate of beat is necessary to maintain the circulation under normal conditions, and this rate may be entirely inadequate when excessive demands are made. The one source of danger in heart-block lies in the fact that during exercise the adaptive increase in heart rate cannot take place. This is more true in the incomplete than in the complete block, for in the former it is possible

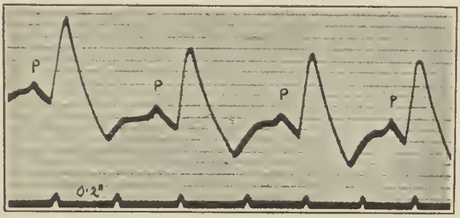
that the block lessens on the removal of vagus influence. Hence, it frequently happens that, although the circulation is carried on efficiently during repose, the patient suddenly succumbs during exertion.

Bundle-branch Block.—Clinical Physiology.—Lesions of the branches of the *A–V* bundle may produce either complete or incomplete block, and these conditions may involve one or both of the bundles, to equal or varying degrees.

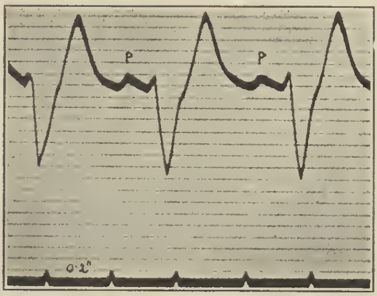
If either the right or left ventricular bundle is completely severed or crushed, so that no impulse can pass, both ventricles still respond; but that chamber to which the bundle has been divided contracts later than the other, for it must necessarily be stimulated *via* the ventricle with the bundle intact. Such alteration in the course of excitation may be suspected to cause alteration in the contour of the electrocardiogram derived from axial leads. That this is so was shown by the earlier work of Eppinger and Rothberger, who found that in leads from esophagus and anus the *R* and *S* waves are replaced by a large and extensive diphasic wave. This wave is first positive and later negative when the left bundle is cut, but first negative and then positive when the right bundle is cut (Fig. 163). The essential features of this experimental work have been corroborated, extended and interpreted by subsequent investigators (Rothberger and Winterberg, Lewis, Smith, Wilson and Herrmann). This experimental work indicates that in complete block of either bundle the *Q–R–S* interval is increased beyond 0.15 second, the deflection is often (though not necessarily) larger and is followed by an exaggerated *T* wave of opposite direction. In complete block of the right bundle in dogs, the initial deflection *Q–R–S* is directed downward in all leads, *i. e.*, the leads are concordant. Occasionally, however, the initial deflection is upward in Lead I, *i. e.*, discordant (Lewis, Smith). In left-bundle lesions the initial deflections are usually upright in all leads and followed by a negative *T* wave. These changes are readily interpreted if we adopt the hypothesis that the *Q–R–S* complex is due to the passage of the excitation wave from endocardial to epicardial surfaces, and that the recorded electrocardiogram is a composite picture of the dextro- and levo-electrocardiogram (*cf.* page 274). In complete bundle block the uninjured side is excited in advance of the others, and this determines the direction of the initial deflection. Thus, if the impulse reaches the right ventricle first the tendency for the waves will be downward; if it reaches the left first, it will be upward. The prolongation of the *Q–R–S* complex is due, in part, to the delay in reaching the injured side and, in part, to the abnormal course which the excitation processes take. Abrupt activation of the injured side may produce a notching or splintering. The *T* wave is conspicuously larger and longer. In right branch block the beginning of *T* is probably a left ventricular effect, and the end is sustained by a right ventricular effect. In left-branch

block the negative T owes its onset to right ventricular activities and its end is sustained by that of the left ventricle.

When both bundles are destroyed (bilateral bundle block) we are apt to have two lower ventricular centers—one on the left and the other on the right—struggling for supremacy as pacemaker (Eppinger and Rothberger, Wilson and Herrmann). In such cases the two pacemakers may act in unison, producing normal complexes; or one side may dominate the heart beat and cause curves in which electrocardiograms correspond to early activity of that side.



a



b

FIG. 163.—Effect of cutting (*a*) left branch and (*b*) right branch of the His-Tawara system on electrocardiogram (leads from anus and esophagus). (After Eppinger and Rothberger.)

Clinical Recognition (Fig. 164).—The most constant aberration associated with clinical branch block is the lengthening of the Q–R–S complex beyond normal. Authorities differ as to the increase necessary before the condition may be suspected, values ranging from 0.1 to 0.2 second being given. Associated with this broadening of the Q–R–S complex are changes in contour and amplitude, due to a lack of balance between right and left ventricular excitation. The change in amplitude, however, is of less importance than the change in contour, as the former depends upon the amplitude of the levogram and dextrograms respectively as well as on their algebraic addition. The initial complex is frequently notched in a way that is

quite distinctive from that observed in normal electrocardiograms (Wilson and Herrmann); whereas, normally, such notching is confined to the smallest lead (usually III) and occurs near the base line, in branch block, notching occurs most frequently near the apex of large upward or downward directed initial deflections (Figs. 164 *A*, *B*).

The bulk of clinical and pathological evidence (Carter, Lewis, Eppinger and Stoerk, Wilson and Herrmann) indicates that, as in experimental animals, the direction of the aberrant initial deflection

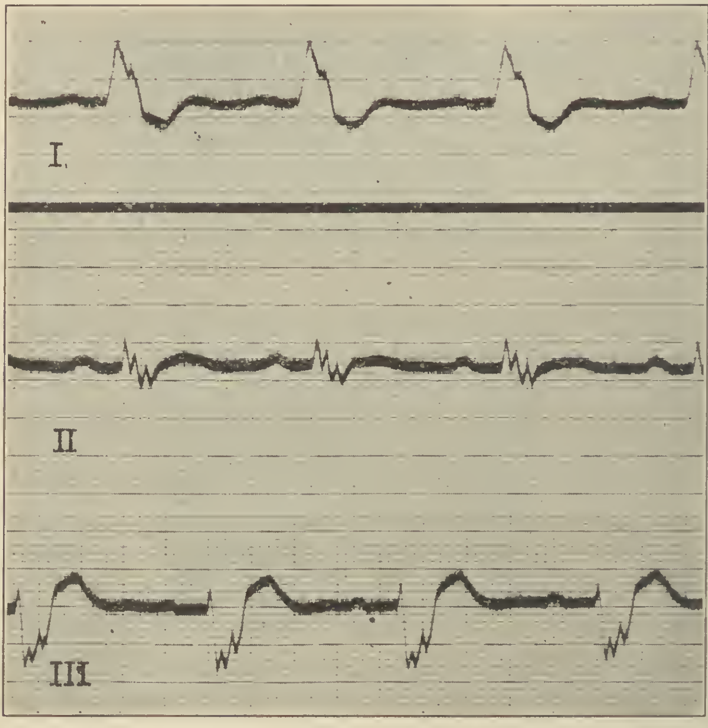


Fig. 164 *A*.—Electrocardiograms (Leads III) from a case of right bundle-branch block in man. (Courtesy of Dr. R. Scott.)

is downward in Lead III in the case of right-bundle defects and upward in Lead III in left-bundle defects. In the latter case, however, the initial deflection is downward in Lead I. A comparison of these observations with those of experimental bundle lesions produced largely in dogs, indicates that certain discrepancies exist as to the leads involved in the predominant upward and downward deflections. In brief, while in dogs Leads II and III are usually concordant, in man Lead II is often unaffected, but Leads I and III are discordant.

These and still other differences are generally explained as due partly to differences in the distribution of the Purkinje strands of the right ventricle (Lewis), partly to the fact that, clinically, these conditions are frequently accompanied by preponderance of one ventricle or the other. In consequence, initial complexes which are transitional between those due to bundle defects and one-sided predominance occur (Wilson and Herrmann). Indeed, the latter effect may be so pronounced as to obscure bundle effects entirely, the initial deflections then indicating typical ventricular preponderance alone.

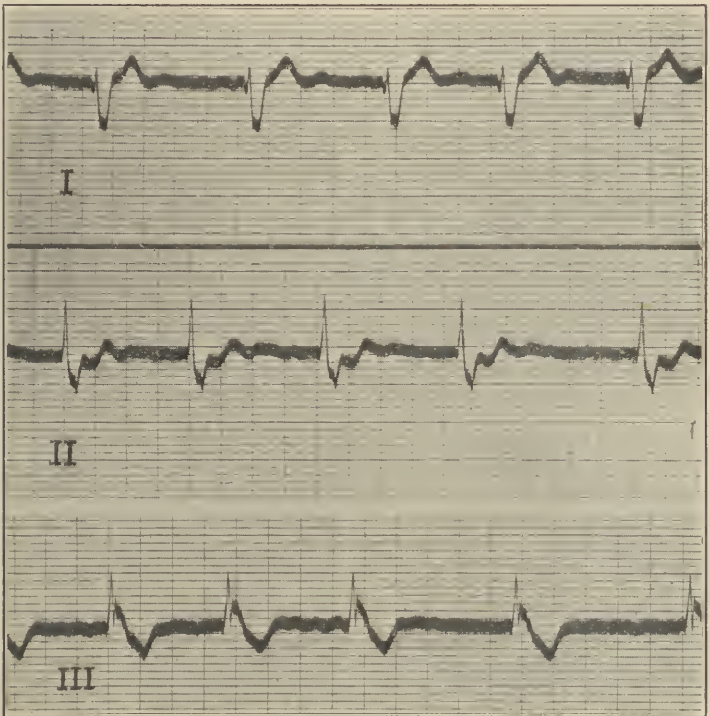


FIG. 164 *B*.—Electrocardiograms (Leads III) from a case of left bundle-branch block in man. (Courtesy of Dr. R. Scott.)

When this happens, the direction of the terminal deflection, *T*, differentiates the conditions; in pure hypertrophy the *T* deflections are normal, while in bundle-branch lesions they not only alter their contour but go in inverse directions from the initial deflection.

While prolonged aberrant initial complexes, which are followed by *T* waves of opposite potential, are commonly regarded as characteristic of *right bundle-branch block when the initial deflection is negative in Lead III and diagnostic of left bundle-branch block when it is negative in Lead I and positive in Lead III,* it has been held, both on theoretical

ground and on postmortem findings, that just the reverse interpretations of records should be made. In this discussion, the theoretical objections deduced by Fahr cannot be weighed heavily, especially as it is just as easy to postulate conceptions that conform beautifully (Wilson and Herrmann, Lewis). Until more is definitely known as regards the spread of negativity and its modification, when conduction is abnormal, no final decision can be based on hypothetical discussions alone. Of more direct significance are the reports of cases in which the electrocardiographic diagnosis does not check with postmortem findings. A number of such reports have shown that definite clinical indications of one-sided block may be unassociated with anatomical findings (Cohn and Lewis, Carter). In such instances we can assume that block is determined by functional rather than by morphological change. This is scarcely possible, however, in the cases reported by Oppenheimer and Pardee, where lesions of the branch opposite from that expected from electrocardiographic studies were found. Until more such cases are reported, however, it seems preferable to refer these isolated instances to changes in the electrical balance of the right and left heart, resulting from coincident, degenerative changes in the myocardium. It is certainly premature to conclude that our entire philosophy as regards the diagnosis of right and left bundle-branch block is wrong. Such discrepancies between anatomical and electrocardiographic diagnosis are sufficient, however, to place the enthusiast on guard in the diagnosis of bundle-branch lesions, as they occur clinically.

The clinical differentiation of incomplete bundle-branch block has not been conclusively established. The experimental work of Wilson and Herrmann seems to indicate that the aberrant electrocardiogram frequently attributed to intraventricular or arborization block (discussed below) may in reality be indications of incomplete bundle-branch block. The entire question may, however, be said to be in the stage of patient observation.[1]

Arborization Block (Intraventricular Block).—That block due to functional, toxic or degenerative changes may occur in the terminal arborizations of the Purkinje system and so cause abnormalities in the spread of the excitation wave through the ventricles is a possibility that must be considered. In 1916, Oppenheimer and Rothschild described a series of cases in which extensive patchy sclerosis and fibrosis of the endocardial and subendocardial layers were found associated with electrical variations of a peculiar character. The Q–R–S complexes were prolonged (0.1 second) and the R wave was notched or splintered and of small amplitude. The curves differed from bundle-branch block in the absence of a diphasic curve (negative T). Similar cases have been reported by Carter, Willius, Neuhof,

[1] A review of cases with probable delayed bundle conduction, together with an analysis of a new case has recently been made by Korns (Arch. Int. Med., 1922, **30**, 158).

Wedd. This condition has been termed *arborization block*. The disturbance may be permanent, in which case it has been presumed that degenerative changes are operating; or it may be temporary and changeable, in which case functional block at the arborization has been supposed to occur (Robinson).

Experimental Physiology.—Arborization block is difficult to produce directly, owing to the difficulty of dividing successfully even the majority of terminal arborizations. Such observations as have been reported, however (Eppinger and Rothberger, Wilson and Herrmann), indicate that cutting of a large portion of the terminal arborization produces very minor changes in the axial electrocardiogram, and that these do not resemble changes attributed, in clinical cases, to arborization block. Such lesions, however, do not involve the final arborizations as definitely as in man. Attempts have, therefore, been made to reduplicate these lesions by ligating various branches of the coronary arteries (Smith). In such cases, changes in the initial deflections corresponding to those obtained clinically were rarely obtained; but the chief effects were on the T waves, which became negative and then iso-electric. These experiments are probably more comparable to clinical conditions, since they reproduce almost exactly the findings reported in clinical cases. The failure to obtain corresponding curves in these experiments tends to show that the deflections described as characteristic of arborization block are at least not entirely produced by extensive degenerative changes. Wilson and Herrmann further point out that, owing to the extensive arborization found in the ventricle, only a very extensive involvement of arborizations can be expected to effect the conduction of impulses to the ventricular muscle. As previously indicated, these investigators are, therefore, inclined to attribute such cases to incomplete bundle block. Complying with these observations, Drury as well as Herrick have reported cases in which extensive subendocardial degenerative changes were found, but no typical alterations of the initial electrocardiographic deflections were obtained prior to death. The possibility that the few remaining pathways still open may become functionally blocked and really cause such waves must, however, be considered, especially as Smith has more recently shown that a combination of coronary ligation and fatigue (?), caused by forcing the ventricle to beat in the partially closed hand of the experimenter, produced such splintered waves. For the present, the significance of splintered and broadened initial complexes as a criteria of arborization block must be considered *sub judice*.

VIII. ALTERNATION OF VENTRICULAR CONTRACTIONS.

Definitions.—Since its recognition by Traube, in 1872, the term *pulsus alternans* has been applied clinically to that variety of bigemi-

nal pulse in which the smaller waves are not of longer duration than the larger ones. The term has, however, also been frequently applied to a condition of the heart in which strong and weak contractions alternate. Strictly speaking, it is preferable to refer to this condition as *ventricular alternation*. Such ventricular alternation may not produce an alternation of pulse amplitude, however, *e. g.*, either when the degree of alternation is so slight that it does not affect the peripheral pulse, or when it is so extreme that no ejection occurs and only a slow pulse (*i. e.*, a half rhythm) is felt in the peripheral vessels.

Pathological Physiology.—Experimental alternation of the heart has been produced under a variety of conditions. Among these may be mentioned: (*a*) An inherent predisposition, which develops during prolonged exposure and manipulation; (*b*) an alteration of the quality or quantity of blood supply, subjecting the heart muscle to deleterious chemical or physico-chemical influences; (*c*) ligation of the coronary vessels; (*d*) increasing the frequency of the heart beat; (*e*) nervous influences, *e. g.*, accelerator stimulation (Hering). Finally, it has been produced by many chemicals and drugs, such as glyoxalic acid (Adler, Hering, Kahn and Starkenstein), aconite (Cushny), digitalis and antiarin (W. Straub), veratrine (Hedblom) and possibly chloroform (Kaufmann and Rothberger).

The condition so produced in the exposed heart has been studied, both in amphibian and mammalian hearts, by inspection as well as by all forms of mechanical registration, *e. g.*, by the suspension method, by the myocardiograph and by intraventricular pressure and arterial pressure curves. In recent years it has been especially studied by use of the electrocardiogram and heart sounds.

The results of inspection and graphic registration indicate clearly that the alternation may affect different portions of the heart singly or together. It has been observed alone in the auricles or ventricles, or may involve all chambers. The alternations in different portions (*e. g.*, auricle and ventricle) may be concordant or discordant and, according to some investigators, discordant beats may occur in different portions of the same ventricle (*e. g.*, apex and base). Again, contractions in one region may be equal from cycle to cycle and in another alternating.

While such observations are of great significance as bearing upon the ultimate nature and cause of alternation, clinical physiology is chiefly concerned with the total effect of such changes in the ventricles of mammals, where no such regional differences have been demonstrated by faultless methods. Dynamic studies, by means of manometer apparatus and the registration of heart sounds, indicate that the weaker beats are characterized by a slower rate of contraction, a longer isometric phase, a reduced phase of systolic ejection and a decrease in the systolic discharge (Kahn, Kahn and Starkenstein, Straub).

Electrograms and electrocardiograms present a variety of results. Alternation in both *R* and *T* deflections may occur concordantly with mechanical alternation or they may be discordant. In some cases the *T* wave may be predominantly or solely affected, but *R* is never affected without *T*. Occasionally, *R* and *T* may be oppositely affected, *i. e.*, *R* may decrease and *T* increase during the larger mechanical beats. Finally, no electrical alternation may be evident. The heart sound records show distinctive changes. In the weaker beats, the first sound is usually of smaller amplitude and may be shorter in duration (Kahn). Not infrequently, the second sound is lacking entirely in the smaller contractions. The interval between sounds is greatly reduced in the smaller beats, indicating an abbreviation of systole.

Nature of Alternation.—Many experimental attempts have been made to elucidate the fundamental nature of this condition. Two views are still held: (*a*) That it is due to a periodic variation in the contractility or irritability of all the cardiac elements, so that they contract to a maximal extent only during every alternate beat, *i. e.*, that a condition of total hyposystole periodically recurs (Wenckebach, Fredericq, Hoffmann); (*b*) that it is due to the periodic elimination or depression of certain fractionate contractions. Most of the experimental work favors this latter interpretation. According to this conception, it may be supposed, moreover, that certain muscle fractions fail to contract in their entirety (partial asystole) (Gaskell, Englemann, de Boer, Kisch, etc.) or that their contractile function is merely reduced (partial hyposystole) (Hering). There is also some difference of opinion as to why these fractions fail to contract. This may conceivably be due to a reduced irritability of certain muscle units, rendering the natural impulse subminimal (Gaskell, Cushny) to a periodic conductivity disturbance producing a local block (Englemann, Muskins), or to the fact that certain fractions have a long refractory phase (Mines, Lewis). Mines has called attention to the fact that a marked alternation of the electrocardiogram may exist in the absence of apparent mechanical alternation and has offered a plausible explanation of such potential alternation. According to his interpretation, the larger beats do not necessarily represent a contraction of the entire ventricular musculature. Thus, if we call the entire musculature V and the non-contracting fractions v, the visible alternating contractions may not be expressed simply as V, V–v, V, V–v, but more probably as V–v_1, V–v_2, V–v_1, V–v_2. In other words, certain fractions may be subtracted from both contractions. In proportion as v_1 is smaller than v_2, so the height of alternating contractions will vary. If v_1 and v_2 are equal, only a potential alternation exists which is not recognizable mechanically, but, owing to their different position in relation to electrodes, may produce dissimilar effects on the electrocardiogram.

According to this hypothesis, it is possible to explain why a prolonged rest period may intensify the alternation by transferring the non-conducting elements to the other beat, thus: V, $V-(v_1 + v_2)$; V, $V-(v_1 + v_2)$. In this way, what is gained by one beat is lost by the other.

Clinical Recognition (Figs. 165 and 166).—The condition was first recognized by the alternating heights of pulse waves (Traube), but has been frequently confounded with bigeminal pulses, due to recurring premature contractions. These two conditions may be distinguished by the fact that the beats in pulsus alternans either recur regularly, or if any slight variation does occur the larger beats occupy a somewhat longer interval. This probably occurs because the period of isometric tension of the preceding smaller beat is longer. In the case of premature systoles, on the contrary, the intervals are never equal, and the smaller beats occupy the longest interval. It may happen that the condition is complicated by premature con-

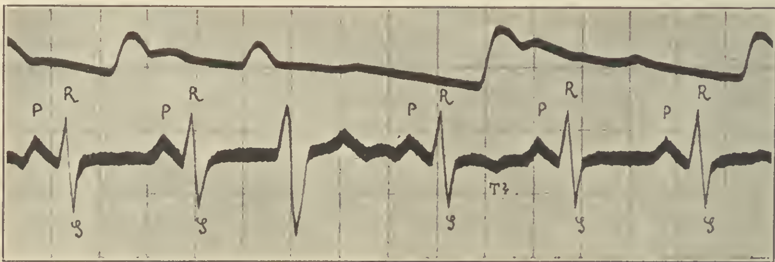


Fig. 165.—Radial pulse and electrocardiogram in case of pulsus alternans complicated by ventricular premature systole (third e, c y wave). (After Kahn.)

tractions, in which case characteristic complexes are found in the electrocardiograms without evidence of their occurrence being present in the arterial pulse (Fig. 165).

The electrocardiogram shows a normal sequence of P, R and T waves. Variations in the duration of systole and diastole are usually not present, indicating that the pulse variations may not be a true criterion of the actual length of the cardiac cycles. The waves may show alternations in height, which do not always correspond to the pulse variations, however. In many cases, no variation occurs when the pulse shows the alternation plainly, and occasionally an electric alternation may occur without a mechanical variation. This suggests that possibly the electrocardiogram waves are an expression of excitation rather than of contraction. At any rate, the electrocardiogram is not a certain means of recognizing this affection. When premature systoles occur, as in the third complex of Fig. 165, they may be readily recognized by their peculiar contour.

Pulsus alternans may also be associated with other forms of irregu-

larities. It frequently accompanies auricular tachyrhythmia (auricular flutter) as well as paroxysmal tachycardia of the whole heart.

Prognosis.—The existence of pulsus alternans indicates that the heart muscle is damaged or is unable to react to a greater strain. The prognosis, therefore, depends upon the associated disturbance. If we find it present during rapid heart action following exercise or during paroxysmal tachycardia, it may indicate that the muscle is unable to meet the strain for the time being. It is then not of so serious a nature. If, however, the pulsus alternans comes on during normal action of the heart, it can be due only to extensive degenera-

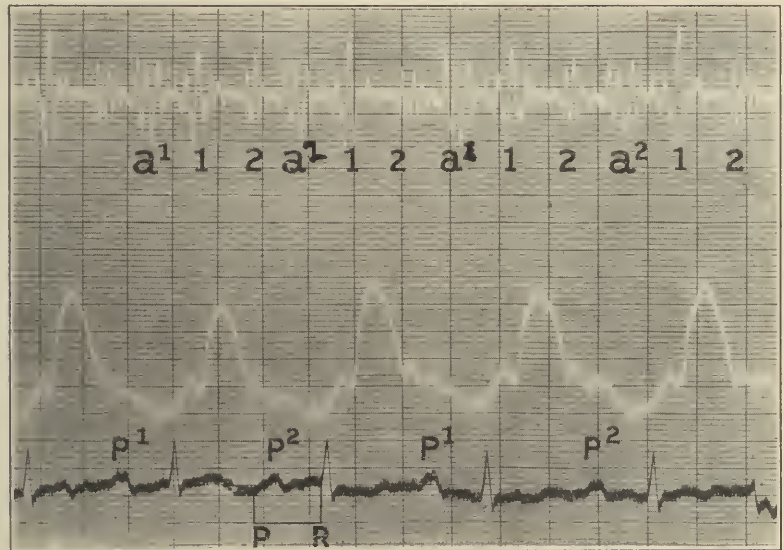


FIG. 166.—Records of heart sounds, carotid pulse and electrocardiogram, Lead II, from a case showing alternation of the ventricles and discordant auricular alternation. Delayed $A-V$ conduction as shown by prolonged $P-R$ interval. a^1, a^2, auricular sounds; 1, 2, first and second heart sounds. Illustrating also the presence of auricular sounds when $As-Vs$ interval is long. Analysis in test. (Courtesy of Dr. Harold Feil.)

tive changes, sclerosis or other involvement of the heart muscle. No hopeful prognosis can then be given, and the danger is even more pronounced if the pulsus alternans is accompanied by anginal pains

Alternation of Auricular Contractions.—As already indicated, alternation of auricular contraction has been demonstrated experimentally. Furthermore, it may be either concordant or discordant with a simultaneous ventricular alternation or may occur alone. Its diagnosis has not been placed upon a very sound footing, however. As a rule, attention has been directed to alternation in the size of the *a* wave of the venous pulse (Volhard). As Rihl has pointed out, however, it is quite precarious to base a diagnosis of auricular alternation on the

evidence of such variations alone, since they may result from the variable resistance offered to the venous inflow when it is associated with ventricular alternation.

A clear-cut demonstration that auricular alternation may accompany ventricular alternation in man is offered in the graphic records of Fig. 166. For this tracing, as well as the privilege of its analysis, I am indebted to Dr. Feil. In this instance, ventricular alternation, as evidenced from the pulse tracings, is accompanied by an unusually prolonged *As–Vs* interval, as indicated by the greatly prolonged *P–R* interval in the electrocardiogram. This has the effect, as previously analyzed (page 325), of producing an auricular sound, but, in this case, of rather unusual amplitude (Fig. 166, a_1). Careful inspection of this record shows, moreover, that the auricular sounds (labeled a^1), which precede the feebler first sounds of the smaller ventricular beats are of larger amplitude than those auricular sounds (labeled a^2), which precede the larger ventricular first sounds. This, taken together with the fact that the *P* waves, corresponding to the louder auricular sounds, are also somewhat larger and tend to display a slight degree of alternation, may be regarded as demonstrating that discordant auricular and ventricular alternations exist.

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CHAPTER XXIII.

THE DYNAMIC CONSEQUENCES OF ABNORMAL CARDIAC RHYTHMS.

ALTHOUGH the greatest interest in abnormal cardiac rhythms has centered upon questions as to their causations, interpretations, diagnosis, prognosis and their relations to myocardial involvement, their effect on the dynamics of the circulation is of no less concern to patients and physicians as well. The normal cardiac mechanism is particularly well adapted to maintain not only an adequate transfer of suitable blood volumes from the venous reservoir to the arteries, but to supply a constant and sufficient stream to the body cells as well. If, for any reason, the normal rate or coördination of the heart beat is seriously interfered with, more or less serious circulatory derangements must result unless compensatory mechanisms operate to restore the circulatory balance. It is, therefore, desirable to follow, as logically as our present knowledge will permit, the primary disturbances occasioned by abnormalities of cardiac rhythm and to consider the compensatory mechanisms that are called into play. In attempting to do this, the reviewer is at once impressed by the many gaps which exist in the relatively scanty literature on the subject. These the author has attempted to fill in, as far as possible, by incorporating certain results obtained in experiments which have never been published.

The Effects of Tachycardia and Bradycardia.—The fundamental effects of acute changes in heart rate are well understood. In laboratory experiments, slowing is accompanied by a fall of mean arterial pressure, and such acceleration as can be induced by physiological means invariably causes a rise. If the change in rate is a permanent one, a new blood-pressure level, higher or lower than normal, is finally found. These effects are due to the fact that the minute volume discharged by the heart increases and decreases with the rate. If a condition of pronounced slowing or acceleration is maintained for a still longer interval of time, the pressure gradually tends to return to normal. These changes are usually attributed to compensatory phenomena on the part of the vasomotor apparatus.

Such mean pressure observations give us far from a complete or even adequate conception of the circulatory changes involved. We may recognize *immediate*, *stabilized* and *compensated effects* of heart-rate changes. The immediate effects extend over only a few beats,

If the ventricle slows markedly for any reason whatsoever, the diastolic pressure at once declines and the systolic pressure rises for a number of beats, thereby greatly increasing the pulse pressure. Tish is due to the fact that the systolic discharge of the heart increases (*cf.* page 116). Such effects are also produced in all forms of casual, temporary or periodic slowing of the heart in man, and unless the heart stops, no symptoms of cerebral anemia take place. If the slowing continues, however, for more than four or five beats the stabilized period sets in. The systolic pressure then likewise declines and, the more, the greater the slowing. The fall of blood-pressure thus occasioned by permanent slowing may cause cerebral anemia. If the slow heart rate persists for still longer intervals of time the compensatory stage sets in. This consists in an elevation of both systolic and diastolic pressures; sometimes the diastolic pressure increases relatively more, indicating progressive vasoconstriction, at other times both pressures increase equally; or, again, the systolic pressure increases more than the diastolic, indicating an augmented systolic discharge. The latter is due, in part, to increased venous pressure in the auricle and ventricle, which causes not only the expulsion of larger volumes[1] but a greater velocity of ejection (*cf.* page 117). This explains why patients with very slow hearts as permanent phenomena may lead uneventful lives as far as circulatory symptoms are concerned.

The essential cardiodynamics underlying an increase in heart rate have been clearly analyzed by Henderson. The more the heart rate increases the more the period of diastolic filling is cut short, and the smaller is the systolic discharge of the beats. As shown, schematically, in Fig. 38, however, the systolic discharge is only slightly decreased as long as the period of rapid inflow is not encroached upon, *i. e.*, until a cycle length of about 0.08 to 0.1 second is reached. Consequently, at all heart rates up to 60 or 78 per minute the minute volume increases proportionally to the heart rate. Between 78 and 210, each systole encroaches upon the phase of rapid inflow, and while the minute volume still increases with ascending heart rate, it no longer increases proportionally to the heart rate. Above 210, the minute volume progressively decreases until, when a ventricular rate of 340 to 360 is reached, no time for filling is left and the heart goes into a state of cardiac tetanus (Henderson), during which no ejection is possible.

Physiological observations indicate that this fundamental law also governs the systolic discharge and minute output in tachycardia observed in man. Thus, Hooker and Eyster recorded a fall of systolic arterial pressure and an increase of venous pressure with signs of cyanosis in paroxysmal tachycardia. Barcroft, Bock and Roughton, in a similar case having a heart rate of 200, found the minute output

[1] *Cf.* also C. Tigerstedt (Acta. med. Scand., 1922, **56**, 510).

decreased from 6.1 liters to 2.1 per minute, and the systolic discharge diminished from 77.5 to 12.9 cc.

More than occasionally no circulatory embarrassment is seen, however, in extremely rapid heart rates. There are clinical cases of tachycardia in which ventricular rates of 230 cause a definite increase in both systolic and diastolic pressures. Lewis reports a case in which a ventricular rate of 290 in a child caused no circulatory embarrassment, and Korns has just called my attention to a similar case observed by him at Lakeside Hospital. As tachycardias, induced in animals by rhythmic stimulation of the auricle or by flutter, also seem to have a paradoxical effect on blood-pressure—sometimes elevating it, at other times causing it to fall—it is pertinent to inquire into the cause of these phenomena. So far as my observations on experimental animals go, auricular flutter causes an increase of arterial pressure only when the arterial pressure at the onset is relatively low; in all other cases the mean arterial pressure distinctly falls. Two types of records in auricular flutter are shown in Fig. 167. In the upper set of tracings, I and II, the arterial pressures were definitely increased when the ventricles began to beat at a rate of about 350; the lower set of tracings, III and IV, the mean pressure fell distinctly, although the ventricular rate then was only 275 per minute. The arterial pressure records show a fall of systolic pressure, but an increase in the diastolic pressure (no doubt due to abbreviated diastole).

The changes in the intraventricular pressure curves are interesting, but their analysis gives no evidence of any different cardiac mechanism in the 2 cases. Of incidental interest is the fact that, in spite of a greatly abbreviated diastole, the initial intraventricular pressure is significantly lower in the case of the left ventricle.[1] As this takes place in spite of a decreased period of inflow, it can only be interpreted as due to a greater degree of relaxation, *i. e.*, a decrease in tonus. The initial pressure in the right ventricle, on the contrary, increases (y y), due, we may suppose, to a greater inflow of blood on the venous side and a lesser degree of tonus change in this chamber.[2]

In cases of pure flutter the amplitude of the contractions, as well as the spacings, are equal for successive beats (upper tracings), while in slightly impure flutter, considerable variations may occur (lower tracings). This irregularity in the pressure maximum, as well as in the discharge, is not the cause of the fall of pressure, however, for the arterial curves show that the systolic pressure would still be lower even if all beats were of maximal amplitude. The intraventricular pressure maximum, or top of the curve, as well as the volume ejected (as judged from the arterial pressure curves) does not necessarily depend upon the initial pressure, but is apparently determined by the period of diastolic rest. This is instanced by comparing

[1] *Cf.* points labeled X–X in Fig. 157.

[2] This, the only interpretation warranted from the small number of records on hand, is subject to critical reconsideration.

waves 1 and 4; the longer these periods (wave 1) the larger the contractions become.

Searching further for factors which may prevent an actual reduction of minute discharge at rates where it should theoretically occur, a study of the variations of the consecutive phase of the cycle was

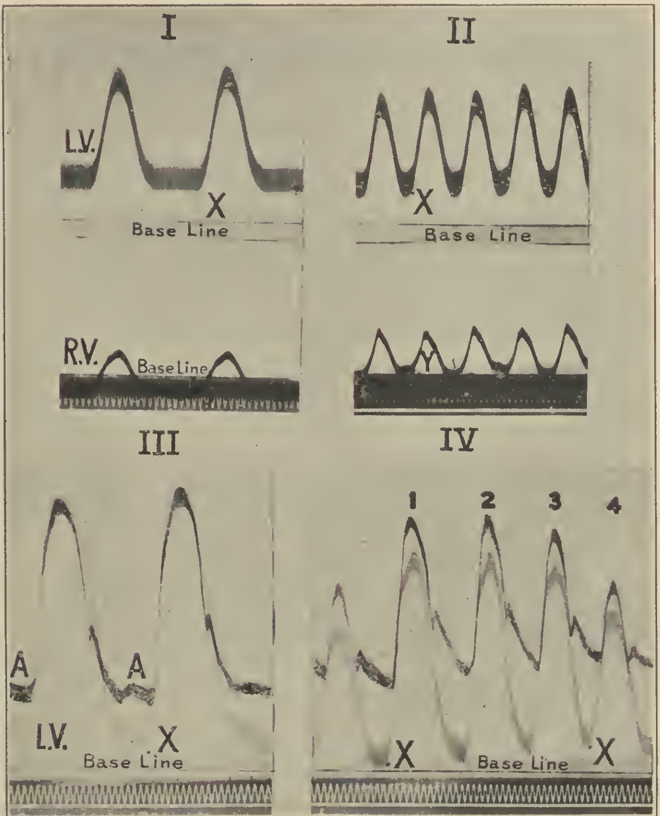

Fig. 167.—Upper curves, right and left intraventricular pressure curves: *I*, normal; *II*, during auricular flutter. Lower curves, left ventricular and aortic pressure: *III*, normal; *IV*, during impure auricular flutter. *LV*, left ventricle pressure; *RV*, right ventricle pressure; *A*, aortic pressure; *X*, initial tension in left ventricle; *Y*, relative initial tension in right ventricle. Time in 0.02 second.

undertaken. Katz and the author have calculated that, according to theoretical volume curves, the following durations of systole and diastole should approximately hold:

Rate.	Cycle length.	Systole.	Diastole.
300	0.2	0.90	0.11
200	0.3	0.135	0.165
150	0.4	0.1575	0.2425

The writer has further shown that, between the end of systole and the opening of the A–V valves, two phases occur viz.: protodiastolic and isometric relaxation phases (Fig. 29, D to F), which together occupy from 0.072 to 0.08 second. If the heart beats according to an unvarying standard, this leaves only 0.03 of a second for filling when the heart rate is as high as 300. This is actually about the filling time (0.032 second), available in the smaller beats, *IV*, of Fig. 167 (lower tracing), while in the upper record this interval is even less (about 0.023 second). It is most remarkable that, within this short filling interval, the heart is able to fill and expel as large systolic volumes as it evidently does in this case. One cannot escape the conviction that the velocity of inflow must have been considerably augmented (possibly by the reduced tonus above mentioned) in order to accomplish such results, even when the arterial pressures are very low. As will be later indicated, such a filling interval is not sufficient in the case of premature systoles to cause any effective beats under any condition.

In some instances, however, the estimated filling time is much longer than anticipated, reaching a figure of 0.053 to 0.06 second. This is indicated in the following table:

	Normal cyclic phases.				Cyclic phases in flutter.			
Experiment.	Systole.	Protodiastolic and isometric relaxation.	Total filling period.	Total diastole.	Systole.	Protodiastolic and isometric relaxation.	Total filling period.	Total diastole.
C 268, VII . .	0.175	0.075	0.127	0.202	0.120	0.062	0.060	0.122
					0.117	0.062	0.032	0.094
C 282	0.124	0.046	0.180	0.224	0.093	0.045	0.023	0.068
C 283, III . .	0.158	0.072	0.462	0.534	0.110	0.052	0.053	0.105

This added time for filling can only be gained in two ways: Either the duration of systole must decrease more than anticipated or the phase of isometric relaxation must decrease. Katz and the author have shown that the former happens in acceleration, due to sympathetic stimulation, and it may be a mechanism which helps filling in tachycardia of sympathetic origin in man. In experimental flutter, such shortening of systole is also indicated in the few experiments in which it could be calculated (see table above). It is possible that this is due to the decreased initial tension, and that this in turn may be associated with less efficient auricular contractions. It is interesting to note in this connection that Katz and Feil have recently found a similar abbreviation of systole in clinical auricular fibrillation and independently arrived at the identical conclusion viz., that the abbreviation of systole is due to failure of synergic auricular contractions to increase initial intraventricular tensions. Be the cause what it may, such observations indicate that, in some instances at least, the abbreviation of systole is a factor which makes a period of ventricular filling possible at very rapid rates. This very interesting subject is open, however, for further investigation.

Frequently, only small increases in heart rate may cause dizziness or actual syncope in patients. This is especially true in paroxysmal flutter when the ventricular rates may not be greater than 150 (Lewis). This is the more curious since, as shown in the table compiled by Katz and the author, diastole then has a length of 0.24 second, and the period of ventricular filling must be nearly 0.16 second. Theoretically, such intervals are quite sufficient for maintaining the minute volume. A study of many volume curves obtained by Katz and the author show that the hearts of experimental animals which have undergone long strains occasionally also show such an effect. As the venous pressure is elevated in these experiments, ventricular impairment is scarcely to be thought of, nor is it indicated in the volume curves. An increase in the duration of systole might possibly occur, however, and actively abridge diastole to an abnormal degree. Thus, suppose that a rate of 200 per minute, the systole increases from its theoretical value (0.135 second) to 0.165 second. In such event, only 0.05 second would be left for filling, and the systolic discharge must necessarily decrease. An increase of venous pressure has been found to cause such a lengthening of systole by Wiggers and Katz. While such a cause may operate in cardiac cases complicated by valvular lesions, I have not observed it as a primary change in pathological tachycardias (*e. g.*, flutter in animals). The most frequent change in such cases is an incompleteness of ventricular ejection. The volume curves do not decrease as much as normally, and the intraventricular pressure curves show a more gradual rise and lower systolic summit. Such changes can only be attributed to a depression of contractility. On the basis of experimental observations, we can, therefore, only conclude that *an increase in heart rate up to 150 per minute causes a decrease in blood-pressure only when it is accompanied by a significant depression of ventricular contractility.*

Influence of Premature Ventricular Contractions.—The graphic effects of premature systoles on mean blood-pressure are well known to experimental workers. When they occur occasionally, the continuous blood-pressure record is marred by an occasional dip, indicating a great temporary fall of pressure. Recurring frequently (*e. g.*, every fourth beat), these dips become more frequent and the blood-pressure level, as a whole, is usually said to be decreased because the minute volume is reduced (Eyster and Swarthout).[1] Actually, the variations in blood-pressure are not as extensive as such mean pressure records would have us believe, for these are seriously intensified by the inadequacy of the mercury manometer. Accurate records of systolic and diastolic arterial pressures, by optical manometer, indicate that occasionally premature systoles decrease the systolic press-

[1] *Cf.* also Hoffmann and Magnus-Alsleben.

ure for that beat; but the diastolic pressure is affected much less—it is, in fact, higher during the beat following after it. The degree to which the diastolic pressure falls depends upon the degree of prematurity, for this determines not only the volume ejected but also the time allowed for the fall of diastolic pressure before the postcompensatory beat occurs. If venous inflow is adequate, this may be compensated by the larger discharge of the compensatory contraction following. Consequently, as Eyster and Swarthout point out, the effect on the average levels of blood-pressure is determined almost entirely by the frequency of the premature beats.

The fundamental dynamics of premature beats are best studied by pressure curves taken from the ventricles and aorta or by volume curves of the ventricles. Since they throw additional light on circulatory dynamics in general, a brief summary of the results obtained from a total of eight experiments is incorporated.

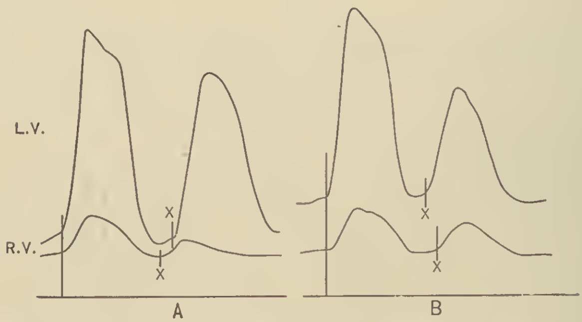

FIG. 168.—Transcribed records of right ventricular, *RV*, and left ventricular pressure, *LV*. *A*, showing right ventricular premature contraction; *B*, showing left ventricular premature contraction. Note difference in time of onset of pressure rise, *X*.

Premature ventricular contractions may arise in the auricle, in the left ventricle and right ventricle. If they arise either in the right or left auricle, the pressure curves begin synchronously in the right and left ventricle and ejection, from the two ventricles, begins simultaneously. In *left ventricular premature systoles*, the pressure in the left ventricle rises in advance; in right-sided extrasystoles, the right ventricular pressure precedes. When this state of affairs exists, from 0.03 to 0.06 second may elapse between the contractions of the two ventricles, and, as illustrated in Fig. 168, an asynchronous ejection of the two ventricles takes place.

Premature contractions may be *effective, i. e.*, cause an ejection of blood and a systolic wave of arterial pressure; or they may be *ineffective* and cause a greater or smaller elevation of intraventricular pressure without opening the semilunar valves. The factors which determine the effectiveness or ineffectiveness of the premature contractions are as follows:

(*a*) The degree of ventricular filling and initial tension determined by: (1) The time interval between the opening of the *A–V* valves and the premature contractions, and (2) the height of auricular pressure and velocity of inflow.

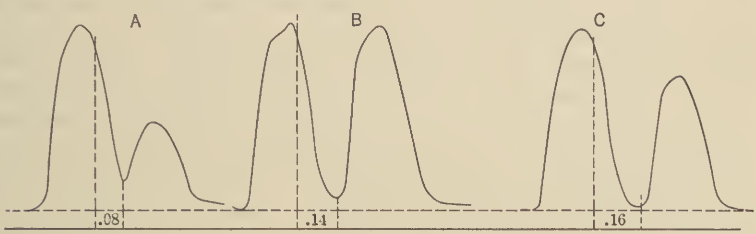

FIG. 169.—Transcribed curves of left intraventricular pressures, showing effects of diastolic rest period, *B*, and initial tension, *C*, on intraventricular pressure. Numerals, intervals between end of systole and premature beats.

(*b*) The height of the aortic diastolic pressure.
(*c*) The diastolic rest period, apart from its effect in (*a*) (1).
(*d*) The vigor and completeness of ventricular contraction.

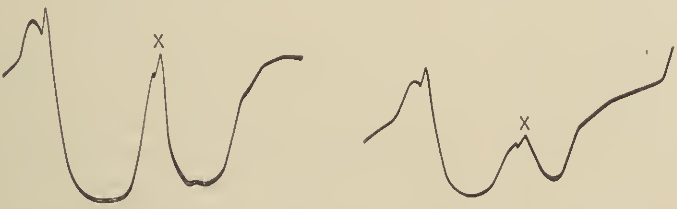

FIG. 170.—Two ventricular volume curves, showing that the magnitude of systolic discharge in premature systoles, *X*, is partly determined by the duration of the influx phase, but also by the completeness of systolic contraction. Systole, downstroke.

By means of the following table and the illustrations in Figs. 169 and 170, the way in which these factors act is brought out. The table also indicates the intervals after openings of the *A–V* valves, in which premature systoles were either effective or ineffective.

		Reaction.	Diastolic pressure.
C 217, VI	0.035	Not effective	173
	0.043–0.055	Just effective	
C 218, XII . . .	0.014–0.016	Not effective	64
	0.082	Very effective	67
C 265, VI C . . .	0.03	Not effective	81
C 268, IV D . .	0.038	Ineffective (but almost effective	
	0.068, 0.08, 0.9	Very effective	68
C 268, VII E . . .	0.04	Very effective	33
	0.06	Less effective	33
C 270, XI B B. . .	0.018	Small but effective	29
C 271, V B. . . .	0.012	Ineffective	46

(*a*) The determining importance of the degree of ventricular filling and initial tension is shown by the pressure curves of Fig. 169. In general, and as illustrated in the first two segments, the amplitude of the premature contraction is determined by the duration of diastole which, in turn, governs the degree of filling and initial tension.[1] Occasionally, however, changes in the rate of filling occur so that an earlier systole may have a higher initial tension. Cases in which the initial tension determines the pressure maximum development are shown in the last two segments of Fig. 169. While the premature systole occurs later in *C* than in *B*, the higher initial tension in *B* apparently determines the greater amplitude of contraction.

(*b*) The influence of aortic pressure is shown by comparing the premature systoles listed in the foregoing table under Experiment C 265, VI *C* (in which a premature systole 0.03 second after opening of the semilunar valves was ineffective) with Experiment C 270, XI *B* (in which a small extrasystole was effective 0.018 second after opening of the semilunars. This is probably the shortest interval at which effective systoles can occur, even when arterial pressures are very low. No systole occurring less than 0.04 second after opening of the *A–V* valves appears to be effective at normal diastolic pressures. Occasionally, a systole as late as 0.055 second is ineffective.

(*c*) That the recovery of muscle, as determined by the length of time after systole, is also a fundamental factor, quite apart from initial tension and ventricular filling, is indicated by the intraventricular pressures developed during ineffective systoles. In such cases the ventricle contracts isometrically and we can get a good idea of the magnitude of the contractile energy developed. Without exception, it has been found that the earlier during isometric relaxation that such contractions occur, the smaller the rise of intraventricular pressure.

(*d*) Variations in the inherent vigor of the cardiac contractions are indicated best by volume curves. While in many cases the systolic emptying of the premature systole is just as complete as normal, it is also frequently found that the emptying is less complete than normal, indicating diminished muscular vigor. This is shown by the two volume curves of Fig. 170.

The Dynamics of Heart-block.—In *A–V* heart-block the fundamental circulatory changes are induced by the slow heart rate. The discussions have largely centered about the question as to whether there is a tendency to compensate by an unusual increase in the ventricular discharges. Clinical evidences favor the view that, during heart-block, the ventricle is able to deliver extremely large volumes—for many cases not far from normal. The writer has notes on a remarkable case, seen some years ago in Bellevue Hospital, in which

[1] *Cf.* also Fig. 170.

a patient with a heart rate of 18 per minute had a systolic pressure of 135 and a diastolic pressure of 68 (some arteriosclerosis and hypertrophy were present, however). It has generally been assumed that such an augmented systolic discharge is due to the fact that each ventricular contraction corresponds to a number of auricular contractions, and that each of these adds an additional increment of blood to the ventricle. On the theory that, in block as normally, the beats of the heart at different rates are superimposable, Henderson has insisted that the systolic discharge of the ventricles in block can be no greater than in similar beats where a coördinated auricular ventricular rhythm exists, the influence of auricular systoles being of no practical account. Gesell has studied this question as an inherent part of an experimental procedure for investigating the importance of auricular systole in ventricular filling, and reached the following conclusions: (*a*) Auricular contractions are most effective in filling the ventricle when they immediately precede ventricular systole; they are less so when the *As–Vs* interval is long; while their effect is zero when they occur synchronously with ventricular systole (*e. g.*, *A–V* rhythm). (*b*) The relative importance of auricular systole is determined by the duration of diastole and the resistance of auricular muscle to stretching (tonus). The author has surveyed these results critically many times, but is somewhat at a loss to understand how they substantiate the idea that the systolic discharge in heart-block is augmented. Katz and the author have not only confirmed the general conclusions of Gesell, but have pointed out that other factors may increase the systolic discharge. We have found the influence of auricular contraction to be variable, depending, in addition to the factors mentioned by Gesell, on the amplitude of auricular contraction. Thus, the amplitude of contraction as well as its contribution to auricular filling is determined by the influence of vagus and sympathetic nerves. In vagal block we quite agree with Henderson that its effect on ventricular filling is quite negligible and becomes more so as stimulation continues. This is well indicated in such volume curves as are shown in Fig. 39, *C*, *D*. . It is doubtful, however, whether such results may unreservedly be applied in the case of structural block, where auricular contraction may be of normal or supernormal vigor. A very pronounced filling effect of a vigorous auricular systole is shown in the first vagal beat of Fig. 39, *B*. An experimental instance of structural block, where each auricular contraction causes an increase of right intraventricular pressure and undoubtedly contributes to its filling and expulsion, is shown in Fig. 171. On the basis of such experimental observations, we can, therefore, not entirely set aside the idea that, in clinical block, each auricular contraction occurring during ventricular diastole aids the filling and discharge of the ventricles to a very considerable degree.

Other factors may also operate to compensate. As a result of

the reduced rate of beat, a smaller minute-volume is transferred from the veins to the arteries, consequently the venous pressure increases in heart-block. This augments the velocity of diastolic filling (Patterson, Piper and Starling, Straub, Wiggers and Katz) and, by further extending the period of systolic ejection (Wiggers and Katz), causes a greater systolic discharge into the arteries.

The Dynamics in Auricular Fibrillation.—In experimental auricular fibrillation the mean arterial pressure curves become very irregular and, as a rule, decrease appreciably (Lewis and Gesell). The minute volume, as determined from cardiometer records, decreases (Eyster and Swarthout).[1] These changes are attributed to various factors, chief among which are: (*a*) The extreme tachycardia, which may exceed the critical rate; (*b*) the presence of large numbers of abortive beats; (*c*) the development of tricuspid regurgitation; (*d*) the removal of the filling function of the auricle. The author has analyzed the question of ventricular rate, the effects of ineffective systoles and the influence of tricuspid regurgitation in detail. Two types of

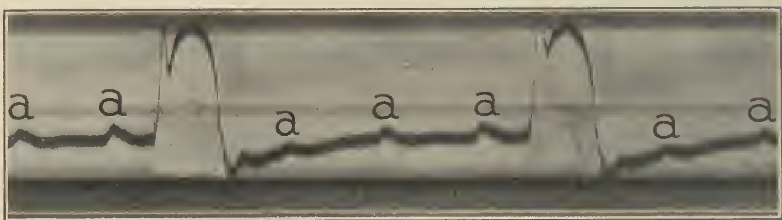

Fig. 171.—Right intraventricular pressure curves, showing influence of auricular systoles during partial heart-block on intraventricular tension. *a*, auricular systoles.

cases may exist, viz.: (1) Those in which a fairly normal arterial pressure is maintained, and (2) those in which the arterial pressure falls and venous engorgement ensues. In Fig. 172, *A*, is shown a case of the former type. The upper record shows the variations in intraventricular pressure from beat to beat; the lower, the corresponding variations in subclavian pressure.

The isometric period extends from *A* to *B*, the ejection period from *B* to *C*. It is evident that systoles varying greatly in strength occur without definite order. The differences in the systoles of different strength manifest themselves in the gradient of the upstroke, in the contour of the ejection period and in the slope of the relaxation curve. The variations in the upstroke and ejection period do not, as in hearts possessing a normal rhythm, depend much upon the initial tension, but more upon the interval between its onset and the end of the previous contraction. The waves occurring immediately after systole are smallest and the rise is more gradual.

[1] Also Hoffmann and Magnus-Alsleben.

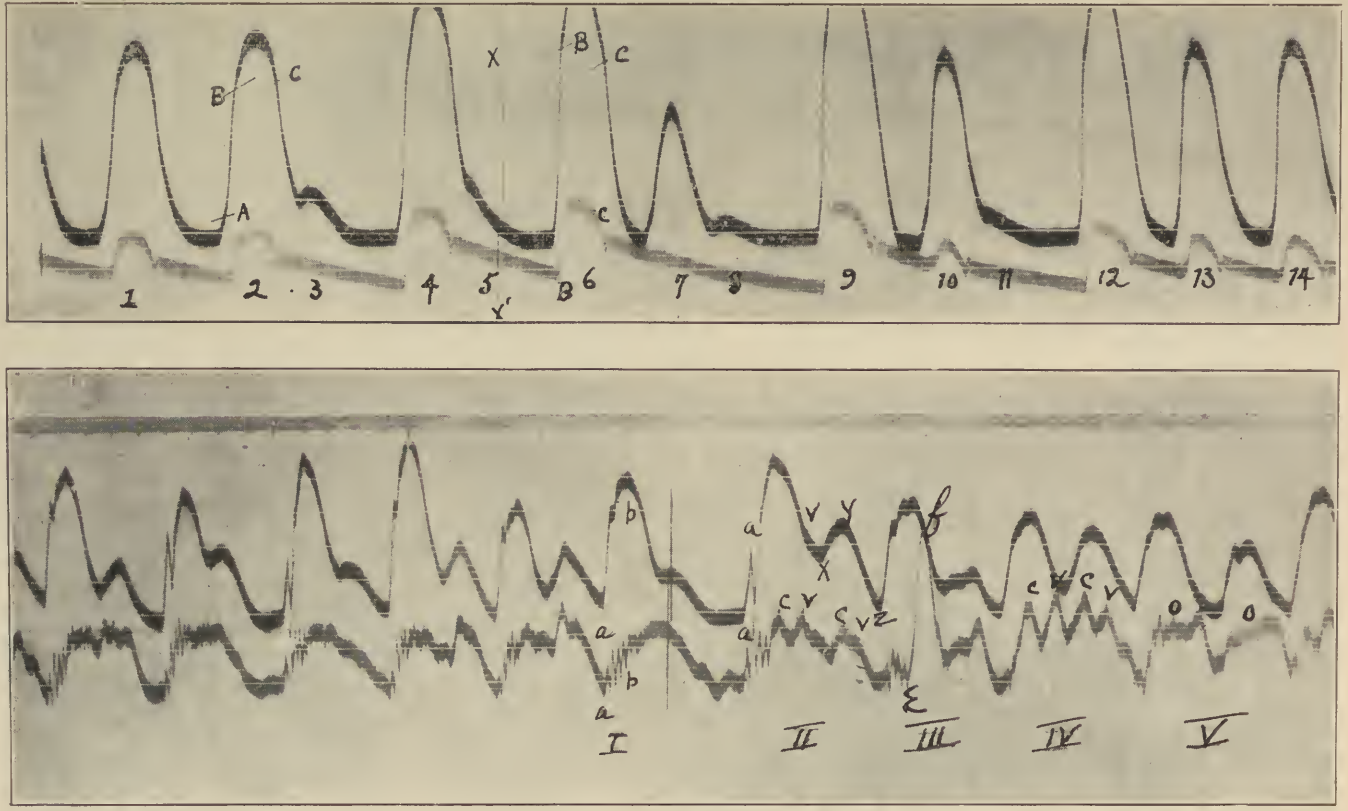

FIG. 172.—*A*, synchronous records of intraventricular (upper) and subclavian pressures (lower) in favorable case of auricular fibrillation in the dog. *B*, synchronous records of intraventricular (upper) and right auricular pressure (lower) in unfavorable case of auricular fibrillation. (Analysis in text.)

Arranging the waves from the smallest to the largest, those numbered 5, 3, 7, 10, 2 and 9 may be placed in a series. When, however, an extra supply of energy is exhausted by two rapidly recurring systoles, the third wave, as at 8 and 11, may be very small, even though a longer interval intervenes. The rate of relaxation is directly related to the strength of systole; partly, at least, because in the weaker beats more blood is retained in the ventricles; partly, also, perhaps, because the inherent rate of muscular relaxation is slower, although no direct evidence for this is obtained.

The pressure of an aortic pulse curve, as well as its shape, depends, to some extent, upon the strength of the ventricular systole, but is also governed by the height of the diastolic pressure at the end of the isometric period of cardiac contraction. Thus, while the gradient of the ventricular upstroke and the height of the curve in waves 10, 13 and 15 are not materially different, the size and shape of the corresponding arterial curves vary extensively. When the semilunar valves fail to open, as in wave 7, no arterial wave is found and the second heart sound fails to occur; while in weaker contractions, such as 3, 8 and 11, no sounds can be heard by means of the stethoscope. This shows that the ventricle may contract and give rise to neither arterial waves nor heart sounds.

Quite a different picture is presented, however, by another class of experiments shown in Fig. 172, *B*. In this experiment the heart was dilated, the venous pressure high and the carotid mean pressure averaged 27 mm. of mercury. The upper curve again represents intraventricular pressure; the lower, intra-auricular pressure. Each group of waves in a heart cycle becomes an interesting study by itself. In Group I it is shown that the ventricle is still capable of giving strong beats. This intraventricular curve appears fairly normal in spite of some regurgitation which is made evident in the auricular curve, both by the sudden rise of pressure during ventricular systole and by the murmur vibration created at *a–b*. In Group II a vibration occurs in the ventricle, which corresponds exactly in time with the first vibration in the auricle. Probably not so much regurgitation occurred in this beat. In the auricles distinct *c* and *v* waves are produced. During the attenuated systole, *x*, *y* and *z* waves, corresponding to the *a* rise and *v* fall, are present. Without an intraventricular pressure curve as a guide, these waves might be interpreted as occurring during the diastole of the previous beat or cycle. The third wave group shows, after a valvular vibration and at the beginning of the ejection period, a sudden rise, *e–f*, apparently indicating that the tricuspid regurgitation was suddenly augmented during the height of the ejection period and permitted a sharp regurgitation. In the fourth group marked out, two weak ventricular systoles caused no regurgitation, but produced a series of four distinct waves comparable to *c* and *v* waves. Similar ven-

tricular contractions may, however, be accompanied by a regurgitation. This occurs in the two waves of Group V, as shown by the immediate and sustained increase of pressure in the auricle as well as by the murmur vibration superimposed at *O*. The chief deviation of the intraventricular pressure curve consists in the slow rate of relaxation which might result from a high degree of tonus or be due to a great accumulation of blood within the ventricle because the average systole takes place with too little vigor. Since the vigor of the systole is dependent upon the frequency of the ventricular contraction, it is apparent that the most efficient circulation is maintained in auricular fibrillation when the beats are initiated somewhat slowly.

Gesell has also studied the influence that an absence of coördinated auricular contraction has on blood-pressure. This he did by inducing auricular fibrillation in hearts where the *A–V* bundle had been crushed and the ventricles were kept beating at a constant rate by artificial stimuli. Under these conditions he obtained a small but definite reduction in mean pressure. These results are of further interest, as they bear upon the question of auricular fibrillation, combined with heart-block, a combination frequently observed. Gesell's tracings show that when the ventricles beat rapidly the induction of auricular fibrillation causes only an insignificant fall of mean blood-pressure (0.6 mm.), but if the rate is slow the fall is somewhat more pronounced (3 to 16 mm.). Further probable evidence that the absence of auricular contractions affects the systolic discharge in clinical cases of auricular fibrillation has recently been adduced by Katz and Feil.[1] These investigators found that in the same individual and at corresponding cycle lengths, the duration of systole is much less when the auricles are fibrillating than when they are contracting regularly. This tends to indicate that initial tension and systolic discharge under otherwise comparable conditions are affected by the absence of synergic auricular contractions.

Ventricular Alternation.—While we have discussed ventricular alternation with cardiac irregularity, this condition is in reality not a disturbance of rhythm but a disturbance of cardiodynamics, in which every second beat ejects a smaller pulse volume. The heart-sound and pulse studies of Kahn and Starkenstein indicate that, in the smaller beats, the duration of systole is decreased and the isometric contraction phase is longer. The changes in right and left ventricular pressure as well as cardiac volume curves have been studied in greater detail by Straub. The chief changes observed are a slower relaxation in the larger beats. This prolongs the isometric relaxation phase and retards the early diastolic filling. As the tempo of the heart is absolutely constant, this slower filling has the effect of

[1] Proc. Soc. Exp. Biol. and Med., 1923. In press.

diminishing the diastolic ventricular volume and, consequently, the subsequent systolic discharge. We may, therefore, suppose that alternation occurs either when the rate is so rapid that the next systole falls on the decline of the pressure curves or when the decline of pressure is so gradual that a similar result is produced. According to the same laws which govern extrasystoles, the second contraction becomes the smaller, the earlier it appears on the descending limb of pressure.

The slow diastolic relaxation is, however, not the only factor concerned, for the curves give distinct evidence that the contraction process is also depressed. The volume curves show distinctly that systolic ejection is less complete in the smaller beat and the intraventricular pressure curves show a lower pressure maximum and slower gradient in spite of an increased initial tension. This can only indicate a depression of the contractile process and can readily be harmonized with the idea that a portion of the muscle elements do not undergo contraction in the smaller beats. In consequence of the slower development of the contractile force, the isometric contraction phase is prolonged and the period of ejection is curtailed. The delayed opening of the semilunar valves explains why the duration of the large beat is longer than that of the smaller one, as calculated from pulse tracings (*cf.* page 508).

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Lewis and Mack: Quart. Jour. Med., 1910, **3**, 273 (*fibrillation on circulation*).

Lundsgaard: Deutsch. Arch. f. klin. Med., 1916, **120**, 481 (*minute volume in total heart-block*).

Straub: Deutsch. Arch. f. klin. Med., 1917, **123**, 403 (*dynamics of pulsus alternans*).

Wiggers: Arch. Int. Med., 1915, **15**, 77 (*dynamics of experimental fibrillation*).

CHAPTER XXIV.

THE VALVULAR LESIONS OF THE HEART.

The normal valvular action upon which the heart beat relies for an efficient transfer of blood from the venous to the arterial channels may be interfered with either by a narrowing of the valvular orifices (stenosis), which offers an added resistance to the flow of blood, or by their failure to close completely (*insufficiency* or *incompetency*), which brings about a backward leakage.

These changes in the valves are usually the after-effects of an infectious endocarditis following the invasion of the blood stream by streptococci,[1] staphylococci, pneumococci or gonococci; or they may be an accompaniment of a general arteriosclerosis, in which case syphilis predominates as the etiological factor. The changes consist of vegetations, scars, ulcerations, fibrous and atheromatous changes, fusion of cusps during reorganization, etc. Finally, valves may rupture during excessive strain or again become insufficient when the ventricles dilate or lose their tonus, in which case the valve rings are stretched and the chordæ tendineæ perhaps become taut before valve closure has been effected. The latter type of lesion is often designated as "functional" as contrasted with "organic lesions," in which permanent morphological changes in the valves are evident.

The presence of fibrosis, atheromatous plaques, rough edges or even vegetations does not necessarily result in insufficiency, for not only smooth sounds but even knotted cords have been introduced experimentally and the valves by their elasticity still adapted themselves to these irregularities (de Santelle and Grey).

It is generally recognized that any valve defect is accompanied by a dilatation of the heart cavity, which leads to anatomical hypertrophy of the cardiac muscle. It is also assumed that such an hypertrophied heart is capable of exerting a stronger beat and discharging a larger systolic output with less call on its reserve force. This has been termed *compensation*. It is not so generally appreciated, however, that the heart is capable of compensating at any time without any increase in muscular development. This is due to the physiologically established fact that the output of the heart per beat or the strength of its stroke is governed by the initial pressure within the ventricle. In experimental work the sudden production of a lesion is followed immediately by an increase in the diastolic pressure

[1] Including the organism causing rheumatic fever.

in the chamber behind, and during the very next beat this chamber responds by a more vigorous contraction. It is very questionable, indeed, whether the subsequent increase in muscular tissue is not a result rather than a cause of the greater physiological activity of which each beat is capable (*cf.* page 570).

AFFECTIONS OF THE TRICUSPID VALVES.

Pathological lesions of the tricuspid valves are comparatively rare, and, when found, are usually associated with other lesions. Why the valves of the right heart are more frequently spared in endocarditis is not fully explained. The most common lesion is a functional insufficiency, which occurs when the right ventricle is dilated, either because it is unable to empty properly on account of a great "vis a fronte," or because its contractions fail. This type of insufficiency has been looked upon as a safety device protecting the right ventricle from excessive distention, and it is often supposed that a relatively small distention is sufficient to cause regurgitation. Observations on experimental animals do not confirm this opinion, however, for their ventricles may be distended under enormous pressures (200 to 250 mm. water during diastole) without causing any regurgitation.

Hemodynamics of Tricuspid Insufficiency.—While tricuspid insufficiency, as recognized clinically, is usually secondary to changes in the left heart or alterations in the pulmonary arterial pressure, the experimental investigations have concerned themselves with the effects of tricuspid insufficiency *per se.* The results of these experiments can therefore, be applied unqualifiedly to only a small per cent of clinical cases.

When the tricuspid valves are rendered insufficient in animals (Rosenbach, Rihl, MacCallum), the pulmonary mean pressure may fall slightly, but the systemic pressure is not appreciably affected unless the lesion is severe and the right heart becomes extremely dilated. The venous pressure rises and the auricular pressure shows a positive wave during systole (Rihl) similar to the ventricular type of venous waves described by Mackenzie.

When the right auricular pressure is recorded by optical manometers, the true character of the waves is shown (Fig. 172, *B*). They consist not of smooth, rounded waves but of fairly sharp increases of pressure, followed by more or less of a plateau, upon which a series of vibrations undoubtedly corresponding to the systolic murmurs are superimposed. Careful study of such waves shows that regurgitation does not become appreciable until systolic ejection begins, furthermore, that it continues into the early phases of diastole, *i. e.*, until the *A–V* valves have opened and ventricular inflow begins.

Clinical Manifestations.—The symptoms of tricuspid insufficiency are chiefly those of cardiac insufficiency in general (*cf.* page 566). They are attributed to venous stasis and a deficient arterial supply to vital organs. The accumulation of blood in the venous reservoirs leads to a stagnation in the liver and portal system as well. This accounts for the symptoms of tenderness over liver, reflex abdominal rigidity, jaundice, anorexia or even nausea and vomiting. The secretory and motor activity of the entire intestinal canal is apparently interfered with, as is shown by the persistent accumulation of gas. Venous stasis and the slowed current probably also account for the production of edema and ascites because the intracapillary pressure is thereby increased (Starling).

The diminished blood supply in dynamic anemia affects, primarily, the cerebral and medullary centers, giving rise to such symptoms as dizziness, giddiness, forgetfulness, augmented breathing and dyspnea. The heart rate is accelerated by a depression of the vagus center. These symptoms are, of course, not pathognomonic of tricuspid regurgitation but of cerebral anemia of any type.

The renal organs are next affected. The secretion of urine diminishes and its specific gravity becomes high. Albuminuria is frequently present.

Physical Examination.—The face of the patient is often cyanotic, the degree depending upon the venous stasis and degree of anoxemia. In extreme cases, the tips of the ears and nose may become a livid blue. If congestion is less severe, the yellow jaundiced tint may appear in the skin as well as in the sclera. The neck veins are, as a rule, distended and pulsate visibly. A systolic liver pulsation is felt on palpation.

The apex-beat is diffuse and may be outside the nipple line. Sometimes the positive beat is replaced by a negative retraction which, however, has no special significance. The cardiac dulness increases to the right, owing to the distention of the right auricle. Fluoroscopic examination confirms these findings.

Upon auscultation, a soft-blowing systolic murmur is heard over the tricuspid area or, more frequently, over the lower end of the sternum. The murmur of a relative insufficiency is frequently softer than one due to endocarditic changes, but it should be borne in mind that the latter may become very faint when the cardiac contractions become weak. As far as the writer is aware, no records of the murmurs have been reported.

The venous pressure is high, and in the arm may easily reach 25 cm. of water when decompensation is extreme (Hooker). The venous pulse shows a typical variation from normal. It is usually stated that the negative systolic wave is replaced by a positive wave, giving rise to what Mackenzie has termed the "ventricular type of venous pulse." Optical tracings indicate that the contour of the supra-

FIG. 173.—Supraclavicular venous tracing showing various forms of systolic waves during tricuspid insufficiency. *I*, prominent *v* wave beginning to rise eary in systole; *II*, sustained or rising top with murmur vibrations throughout systole. Case of auricular fibrillation.

clavicular venous pulse is entirely changed, however; in fact, several variations may occur in consecutive order when the heart is beating irregularly. Their nature is shown in Fig. 173. Briefly recounted, the curves rise rapidly early in systole and upon their summit are superimposed a series of vibrations resembling those obtained in experimental animals (*cf.* Fig. 172, *B*, and Fig. 173, *II*).

MITRAL INSUFFICIENCY.

Hemodynamics.—The simpler dynamic changes in mitral insufficiency have been studied both in artificial circulation schemes (Marey) and in animal experiments (MacCallum and McClure). In relatively simple experiments with artificial circulation machines, it can be shown that when a mitral valve is rendered insufficient the mean auricular pressure rises and the mean arterial pressure falls. It is

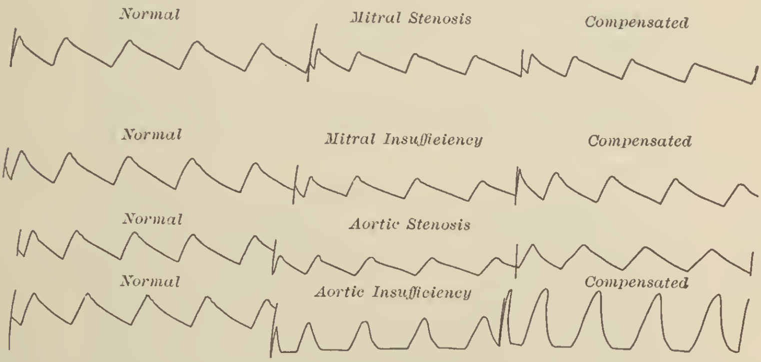

FIG. 174.—Pulse tracings from artificial circulation machine, comparing the effects of different lesions with normal curves.

evident that this is due to a decreased transfer of blood from the venous to the arterial side which, with an unaltered heart rate, indicates a decreased discharge. This decreased discharge accounts for the fact that the amplitude of the arterial pulse is reduced (Fig. 174). It can further be shown that if the stroke is artificially increased in such a scheme, thereby resembling the effect of compensation in the body, the venous pressure is again reduced, the arterial pressure rises and the pulse amplitude returns more nearly to the normal. These simple experiments indicate that the circulatory changes are similar in every respect to the effect of a decreased systolic output of the heart (*cf.* page 580).

These conclusions have, in the main, been confirmed and extended by animal circulation experiments. After cutting or destroying a valve, the carotid pressure falls and the mean left auricular pressure rises. Furthermore, the pressure in the left auricle, instead of decreas-

ing sharply early in systole, now increases very much, as is the case in the right auricle during tricuspid insufficiency. The mean pressure within the pulmonary artery is altered relatively little. With a slight grade of insufficiency it rises slightly, due to a rise of left auricular pressure, but if the insufficiency is great it *falls* (MacCallum and McClure).

In spite of such experimental studies and the application of well-thought-out physical principles, many dynamic questions remain unanswered. For this reason, the author, in association with Feil, recently reviewed the experimental work bearing upon these questions of dynamics and reinvestigated the entire subject by the use of optically recording apparatus not hitherto employed in a study of this lesion.

The Dynamics of the Left Heart and Systemic Circuit.—In discussing the normal mechanism of cardiac action, the closure of the mitral valves at the proper time has generally been considered of crucial importance. By virtue of their complete and secure closure in the earliest moments of systole, the ventricle is able to contract isometrically and, within 0.04 to 0.05 second, elevates the pressure to a level exceeding diastolic arterial pressure, thus insuring prompt and rapid expulsion of blood during the succeeding ejection phase.

How is this rapid elevation of pressure accomplished when the mitral valves are incompetent? What, indeed, prevents all the blood from being expelled through the mitral orifice? How can ventricular tension ever be elevated sufficiently to open the semilunar valves? These and similar questions must be satisfactorily answered.

In 1905, Schwartz, in a philosophical treatment of the subject, came to the conclusion that since considerable regurgitation occurs during the isometric contraction phase, a prolongation of this phase must take place immediately. If the duration of systole remains unaltered, the subsequent phase of ejection must be correspondingly reduced. As a result of this, the interval of systolic discharge must be decreased and some systolic retention must occur. These two events are held to account for the fall of arterial pressures and the dilatation of the left heart. Schwartz pointed out further that the only mechanisms which can truly compensate for such a sequence of events are those that operate to abbreviate the isometric contraction phase again. Schwartz's deductions, however, were not supported by any experimental work of his own.

The results of our experiments demonstrated, however, that, owing to the short duration of the isometric tension increase (0.04 to 0.05 second) and the relatively low average pressure existing within the ventricle (2 to 60 mm. Hg.), very little regurgitation actually takes place; indeed, it was demonstrated by physical methods that this is true even when no valves exist at all, provided the pressure increase

occurs rapidly. This startling fact is well shown by comparing the two tracings shown in Fig. 175, in each of which the darker curve represents volume changes of the left auricle. *C* marks the end of the isometric contraction phase. It is obvious that during the isometric phase the auricular volume increases very little more when the valves are grossly incompetent than when they are competent. Furthermore, this very slight regurgitation affects the gradient of

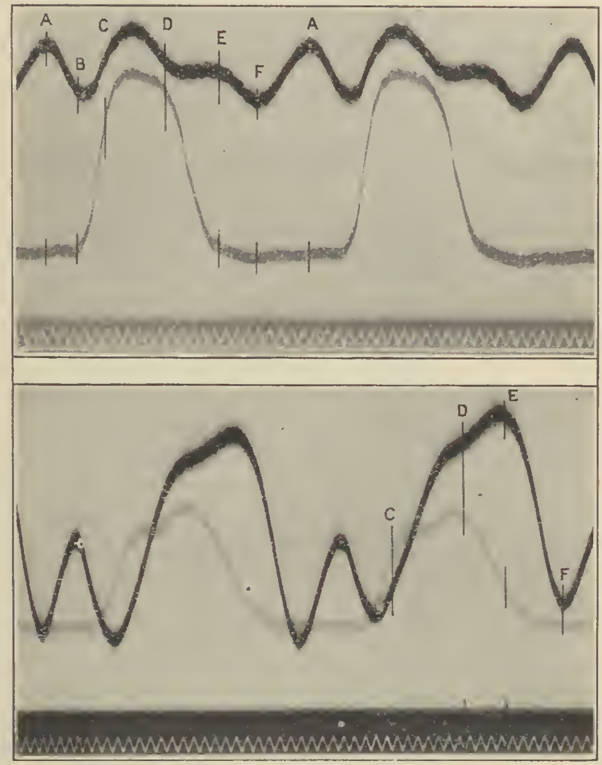

Fig. 175.—Two segments, showing auricular volume-curves (dark curve) and intraventricular pressure curves (lighter curve). Upper segment, normal curves; lower segment, during mitral regurgitation. *C*, beginning of systolic ejection; *D*, end of systole; *E*, beginning of diastolic inflow. Further description in text. (After Wiggers and Feil.)

the intraventricular pressure rises but little, and the duration of this phase remains practically unchanged. Tracings such as those of Fig. 175, furthermore, indicate that while the chief back-flow occurs during the phase of systolic ejection, *C–D*, regurgitation does not cease at the end of systole, continuing about 0.08 to 0.09 second into diastole, *i. e.*, until *E* or where the auricular ventricular valves open and the ventricle begins to fill, *E–F*.

What are the effects of such regurgitation on the systolic discharge and pressures within the aorta? In 1916, Straub studied the dynamics of acute lesions produced by separating the mitral cusps by means of a tiny wire frame inserted through the auricles. His results indicated that during an acute mitral regurgitation there is a marked diastolic and systolic distention of the ventricles, and, to judge from left auricular pressure records, also an elevation of initial intraventricular tension. Stromuhr's records indicated that the output of the left heart is only temporarily reduced and then recovers to normal. Volume curves indicated that the tidal volume entering and leaving the left ventricle during a lesion remains unaltered. Aortic pressures were unchanged.

Unfortunately, Straub, in this series of investigations, employed dynamic apparatus which, at other times, he had submitted to severe criticism. Consequently, his work netted only rough results and left unstudied many vital points that can only be analyzed by the use of optically recording apparatus. Our results, to a considerable extent, corroborated the observations of Straub, with the difference, however, that we reached the conclusion that the tidal volumes entering and leaving the ventricles are increased. In fact, it is by virtue of such a larger tidal volume that the systolic discharge into the aorta is restored to normal. The sequence of dynamic events is as follows: By virtue of this regurgitation, the systolic discharge of the left ventricle is at once reduced and, in consequence, both systolic and diastolic pressures fall, the pulse pressure decreasing (Fig. 176). Since left auricular pressure chiefly increases during the phase of systolic ejection and up to the time when the *A–V* valves open, the filling pressure for the left ventricle becomes greater. Consequently, the tidal volume entering the left ventricle augments (*cf.* Fig. 175). This operates consecutively: (1) To distend the left ventricle; (2) to increase the initial tension; (3) to restore the systolic discharge to normal (Fig. 176). In this way the balance of the circulation is restored within a few beats, in the sense that the systolic discharge of the right and left ventricles become equal again and left auricular pressure does not rise further. It does not compensate in the sense that aortic and left auricular pressures are restored to normal, for once the arterio-venous balance has been upset, the arterial system contains less blood and the left auricle more. If aortic pressures fully recover (which was not the case in our experiment) the peripheral vasomotor apparatus is involved.

It is important to clearly understand the compensatory mechanisms whereby the volume of systolic discharge is returned to normal after a lesion. The higher left auricular pressure and greater diastolic inflow supply a larger tidal volume for systolic ejection. The mechanism whereby the left ventricle is able to expel this larger volume is the increased initial tension within the ventricle. By increasing

the velocity of pressure development, as well as the vigor of its stroke, the larger inflow is actually expelled from the ventricle during systole.

FIG. 176.—Records of intra-aortic and left intraventricular pressures, before and immediately after a lesion. Numerals on time record indicate durations of isometric contraction, systolic ejection and total diastole in each cycle. *x*, points for comparing initial pressures. (After Wiggers and Feil.)

Should this mechanism fail, the systolic residues would progressively accumulate, thus rapidly and fatally dilating the ventricles.

The Dynamics of the Right Heart and Pulmonary Circuit.—During mitral insufficiency the regurgitated blood elevates the left auricular pressure, especially during the phase of ventricular ejection and early diastole. The "back-pressure theory" implies that this increased pressure works backward so that the pressures in the pulmonary artery and right ventricle are also increased and the right heart becomes dilated. On the basis of careful clinical observation Mackenzie has reached the conclusion that such congestion is not the direct effect of valve leakage, but is referred to a coincident myocardial weakness.

On the whole, the results of experimental work have not supported the theory that a mitral regurgitation directly causes a damming back of blood into the pulmonary artery and right ventricle. Bettleheim and Kauders, as well as McClure and MacCallum, found no significant variations of pulmonary mean pressure; indeed, the latter investigators often recorded a slight fall. Straub recorded right ventricular and auricular pressures by membrane manometers and found no demonstrable changes in either their initial or maximum pressures.

Several explanations have been offered as to why the natural equilibrium of the pulmonary circuit and right heart are maintained:

1. The regurgitated blood may be entirely accommodated in the expansile left auricle and its venous tributaries, or new intrapulmonary vessels, may be opened up. This apparently happens after aortic compression in normal hearts, for Straub found in such cases that the volume of the lungs increases without any alteration of pulmonary arterial or right ventricular pressures. According to this conception, which is also favored by Gerhardt, the increased left auricular pressure will affect neither the pulmonary arterial nor right ventricular pressure and volume until the limit of accommodation has been reached in the left auricle and its venous tributaries. In other words, mitral insufficiency *per se* is able to produce no more than a passive *venous* congestion.

2. On the supposition that the reduced systolic discharge of mitral insufficiency causes a smaller volume flow through the peripheral vessels, and consequently a diminished venous return, McClure and MacCallum have suggested that the systolic discharge of the right heart is thereby automatically reduced. This would tend to counteract any tendency that back-pressure effects may have to elevate the pulmonary arterial pressures.

3. Henderson and Prince have shown that in the perfused heart a greater distention of the left ventricle acts to push the interventricular septum to the right, and thereby diminishes the capacity and systolic discharge of the right ventricle. Since the left ventricle is thus distended during mitral regurgitation, it is possible that the pulmonary balance is maintained in this way.

Our observations showed that as long as the cardiac muscle is efficient, the increased volume of blood contained in the left auricle during systolic ejection is accommodated by an expansion of the left auricle and its venous tributaries. Consequently, no "back-pressure" effects are produced in the pulmonary artery or right heart. Our results indicate, however, that this is not prevented by a compensatory decreased discharge of the right heart, either as a result of a decreased return, as suggested by McClure and MacCallum, or by a crowding of the interventricular septum to the right, as indicated in experiments of Henderson and Prince. It occurs, we believe, with undiminished discharge of the right ventricle, because, as Gerhardt suggested, the excessive volume of blood is accommodated by an expansion of the left auricle and its tributaries.

Influence of Altered Circulatory Conditions.—Under altered circulatory conditions, special variations of the following nature were observed: During cardiac slowing, the phase of systolic ejection is prolonged and a larger volume of blood regurgitates into the left auricle. This only temporarily decreases the systolic discharge, for it is compensated quickly by an elevation of filling pressure and an increased tidal volume. When the venous return to the right heart is augmented experimentally, the left ventricle responds with increasingly greater initial and maximum pressures as well as larger systolic discharge up to the levels equal to the average normal heart. The reserve power, if reduced, is undoubtedly still very considerable. When arterial resistance is increased in the systemic circuit, the regurgitation volume increases markedly at once, thereby elevating not only left auricular pressure, but causing also a greater damming back of blood into the pulmonary artery and right heart. During this process, systolic discharge is decreased until initial intraventricular tension has been considerably elevated. When this obtains, the systolic discharges of the two ventricles are again equal and a new stable equilibrium is restored.

Clinical Manifestations.—The symptoms and clinical signs of mitral insufficiency depend, to a considerable extent, upon the duration of the lesion and the condition of the heart muscle.[1]

In incipient cases, as experimental results would lead us to expect, there are no significant disturbances of the circulation and, by consequence, no symptoms and but few signs. The chief sign is the existence of a soft-blowing systolic murmur[2] at the apex (Fig. 177), but inasmuch as this is frequently of accidental origin or purely functional in character, great care must be exercised in making a

[1] For the principles of cardiac diagnosis laid down for the guidance of army medical officers by the Surgeon-General's Office in Circular 21, see addendum at end of Chapter XXV.

[2] For details of graphic records *cf.* page 328.

diagnosis on the basis of a systolic murmur alone. Thus, in an examination of 10,000 recruits, Rothschild found 870 systolic murmurs present, of which only 33 could be attributed with certainty to mitral insufficiency. To judge from our war experience, it appears that physicians err too frequently in diagnosing the condition when

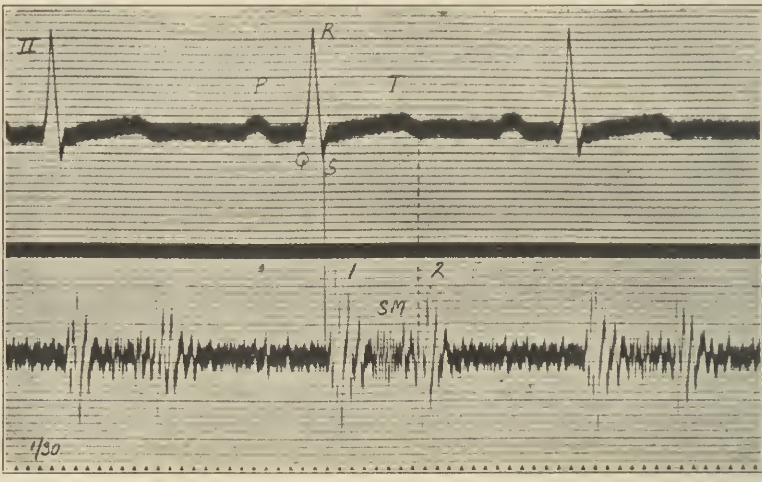

Fig. 177.—Phonocardiogram from case of mitral regurgitation. *SM*, systolic murmur; 1. 2. heart sounds. (After Lewis.)

it does not exist rather than failing to discover the lesion. Connor points out certain characteristics of functional apical systolic murmurs which may be of service in distinguishing them from those due to incipient mitral insufficiency. They may be summarized as follows:

Functional or Accidental.	Organic.
Inconstant, often absent during rest, intensified by excitement or exercise.	More constant.
Localized to apex.	Transmitted toward left axilla.
Character suggests only a modified first sound.	Character suggests added element after the first sound (*cf.* Fig. 177).
Rarely high-pitched, whizzing or blowing.	Usually high-pitched or blowing.

In many instances, these differential characteristics are, however, also of no avail, and then chief reliance must be placed on whether or not an antecedent rheumatic affection was present. It is probably good practice to regard, with suspicion, all systolic murmurs following rheumatic infection; but if, in time, the murmurs persist without cardiac enlargement, they also must be regarded as functional.

In more advanced but compensated cases the circulation may not be embarrassed. Often the only symptom noted is a shortness

of breath when attempting tasks that formerly caused no respiratory distress. As time passes, the signs rather than the symptoms alter. The cheeks become pink, flushed or sometimes even purple. The smaller venules are enlarged. This rosy appearance and bright eyes (mitral facies) give the patient, as viewed by the popular eye, the appearance of excellent health. The radial pulse is often small, but shows no important changes from the normal. As long as compensation is good, it remains regular except, possibly, for an occasional premature systole. The apex tracings show nothing characteristic. The waves may be positive or negative, but no importance can be attributed to a negative record.

It was hoped by clinicians that the registration of esophageal curves might establish the existence of a regurgitant wave into the left auricle. The method is, however, an inconvenient one and the curves thus obtained cannot with certainty be interpreted as showing such a regurgitation (*cf.* page 245).

The systolic and diastolic pressures are not greatly affected (Norris). Occasionally, the systolic pressure is lower and the pulse pressure smaller, which seems to be particularly the case when the heart is rapid.

In addition to the systolic blowing apical murmur, definite evidence of cardiac enlargement is often found. The orthodiagram and roentgenogram show a smooth circular enlargement to the left, involving both the left ventricle and left auricle (Fig. 178). The apex-beat is displaced to the left. Such a complex with a history of rheumatism is characteristic of mitral regurgitation.

Uncompensated or Decompensated Lesions.—If, for any reason, the ventricle does not augment its tidal volume and so compensate for the deleterious effects of valvular lesions, or if compensation once developed fails, due to dilatation, the symptoms and signs alter. This is due to the fact that the blood accumulates in the left auricle and pulmonary circuit, and if the right ventricle similarly fails to perform its function and dilates, a relative tricuspid insufficiency is added. Such cases suffer, therefore, from orthopnea and dyspnea, due, perhaps, in part to the pulmonary congestion and in part to the diminished blood supply to the medulla. The pulmonary congestion, furthermore, gives rise to a chronic bronchitis in which blood-stained sputum is raised in coughing paroxysms. The dilatation of the ventricles often manifests itself by pain over the cardiac region. To these symptoms may *be added all those already described as characteristic of tricuspid insufficiency.*

Percussion shows that the dulness now extends not only to the left but also to the right of the sternum. The orthodiagram shows a uniform enlargement, making the shadow appear like a poorly rounded circle, as shown in Fig. 178. The right auricular border is distinctly enlarged to the right and the pulmonary artery dilated.

The second pulmonic sound is accentuated, indicating augmented pulmonary pressure at the beginning of diastole. The electrocardiogram usually gives evidence of predominant left-sided hypertrophy (*i. e.*, R_{III} is directed downward), thus indicating that any enlargement to the right side is due to dilatation rather than muscle hypertrophy.

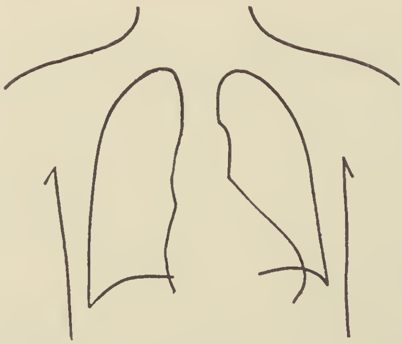

Fig. 178.—Orthodiagram in mitral insufficiency. (After Claytor and Merrill.)

During extreme dilatation, the auricles may give extracontractions or go into fibrillation, thus giving rise to an absolutely irregular arterial pulse. For the details of its interpretation by the aid of the venous pulse and electrocardiogram, other chapters should be consulted.

The arterial pulse waves then are not only irregular, but also unequal in height in such cases. The systolic and diastolic pressures are, therefore, constantly varying and it becomes difficult if not impossible to determine them even approximately.

MITRAL STENOSIS.

Hemodynamics.—It has long been recognized (Vieussens, 1715) that a narrowing of the mitral orifice increases the resistance to the flow from the auricle to the ventricle, thereby limiting the filling and reducing the output. These facts can readily be demonstrated by an adequate artificial circulation machine. After the production of a stenosis, the mean venous pressure rises, the mean arterial pressure falls, and the amplitude of the pulse wave is reduced (Fig. 174). It can further be shown that if the stroke is artificially increased no material changes occur.

Animal experiments have corroborated these findings. If the condition is simulated by tightening a ligature placed around the auriculoventricular ring, or invaginating the auricle into the ventricle with one's finger, or by inserting a small inflated balloon, similar changes occur. The mean arterial pressure falls while the

left auricular and pulmonary pressures rise definitely (MacCallum and McClure). It has been sought to determine, experimentally, the exact effect of stenosis on ventricular filling, by applying a cardiometer to the two ventricles (Hirschfelder). The conclusions and schematic diagrams probably represent essentially the changes in filling that actually take place. Thus, with mild stenosis the inflow during early diastole is slower but is compensated, to some extent, by the more vigorous action of auricular systole. In more severe lesions, the filling occurs very slowly during the entire period of diastole and the total inflow and, consequently, the output during the next systole are reduced. The records published can scarcely be accepted as experimental evidence of these conclusions, however, nor is it probable that the volume changes of the left ventricle can be accurately deduced from volume changes of both ventricles, when their action differs. These conclusions may, therefore, be accepted as theoretical or probable rather than as experimentally demonstrated.

The increase in pressure within the pulmonary artery is commonly supposed to augment the pressure within the right ventricle, to cause its distention and, if it becomes great enough, to produce a dilatation of the tricuspid ring, bringing about a regurgitation. Under these conditions only is the venous pressure raised (Kornfeld); otherwise, it falls, due to the lower arterial pressure. The total quantity of blood within the lungs is apparently increased more than in mitral insufficiency, but the minute flow and velocity of flow are reduced.

Somewhat different results were, however, reported by Straub, who worked with a heart-lung preparation. He too found an augmentation of left auricular pressure, but was unable to demonstrate that the systolic discharge and volume of the left ventricle were reduced, on the one hand, nor that the pressure increased in the right ventricle or auricle, on the other. On the contrary, the maximal right ventricular pressure appeared to decrease. He, therefore, was inclined to regard the incidence of right-sided hypertrophy in clinical cases of mitral stenosis as compensatory in a teleological sense, but arising without primary increase in its work. Similar results were also obtained by Gerhardt, who explains the discrepancies obtained in animal experiments and clinical cases in a different way, however. He believes that in animals, the excess accumulation of blood is accommodated in the pulmonary vessels, peripheral to the capillaries. If, however, the vessels are completely filled at the time a stenosis results—as after saline infusion or after epinephrin injection—then the incidence of a stenosis causes an increase both in pulmonary arterial and right ventricular pressures. Gerhardt concluded that, inasmuch as in chronic heart disease the lungs are already filled with blood, the incidence of a mitral stenosis is sufficient to cause back-pressure effects and an increased work of the right heart, leading eventually to hypertrophy.

Clinical Manifestations.—The symptoms due to mitral stenosis are caused by the pulmonary congestion, dilatation of the ventricle and often relative tricuspid insufficiency. They, therefore, resemble those already described in mitral insufficiency plus, in later stages, those characteristic of tricuspid regurgitation. They make their appearance relatively early in the disease, owing to the fact that the lesion cannot be so effectively compensated by increased muscular action. An interesting complication is the paralysis of the left vocal cord. This is usually assigned to compression of the left recurrent laryngeal nerve by the enlarged auricle, although other explanations have been given (*cf.* Rosenthal, Guttman and Neuhof).

The physical signs of a typical "text-book case" are so characteristic that no difficulty in diagnosis presents itself. The rough

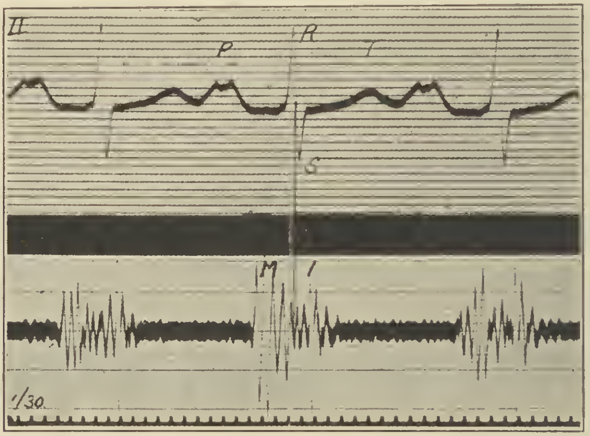

FIG. 179.—Electrocardiogram and phonocardiogram in mitral stenosis, showing large notched *P*-wave and presystolic murmur, *M*. (After Lewis.)

crescendo presystolic murmur, felt also as a thrill and ending in a snappy first sound, which is accompanied by a sharp systolic shock on palpation, are often in themselves distinctive. When combined with an accentuated pulmonic second sound and enlargement of the heart both to the right and to the left, the diagnosis is completed. The nature of the murmur, as shown in graphic records, has already been discussed (*cf.* Figs. 116 and 179).

Nevertheless, erroneous diagnoses of this lesion are common. Thus, Cabot reports that in 200 cases verified by autopsy at the Massachusetts General and Boston City Hospitals, only a little more than 50 per cent were diagnosed correctly. The reasons for this are several. Among army medical examiners, the shock and apical impact, so common in "irritable hearts," were at first frequently interpreted as due to mitral lesions. Connor, therefore, warns that a diagnosis

cannot be made without unmistakable evidence of a presystolic murmur, and points out that a rapid heart rarely occurs. The murmur is often confused with a presystolic murmur present in overactive hearts (Sewall, Morris and Friedlander). This type of murmur is said to disappear in the reclining position and is followed by a reduplicated sound and systolic shock; moreover, the pulmonary second sound is not accentuated. Occasionally, a diastolic murmur accompanies the presystolic, and it may then be difficult to differentiate between a mitral stenosis with a Graham Steell murmur and an aortic insufficiency with a presystolic Flint murmur (Cabot, Goodman, etc.). In such cases the location, transmission, quality and time relations of the diastolic murmur are significant. As shown in the sound records of Figs. 112 and 115, the diastolic murmur of aortic insufficiency falls close upon or even at the time of the second sound; while that of mitral stenosis, which is due to the early filling of the ventricle, is necessarily separated from the second sound by an interval. Furthermore, the type of ventricular preponderance present in electrocardiograms is of diagnostic value; in mitral stenosis, right-sided preponderance is the rule; in aortic insufficiency, on the other hand, left-sided preponderance generally obtains (Fig. 190). At times a diagnosis is missed, owing to the fact that the murmur is not heard. In milder grades it is often fugitive and elusive (Goodman), at times being scarcely audible, at others, harsh and evident. In such cases it may often be brought out by exercise (Pardee), by the use of amyl nitrite (Morison) or by slowing the heart through compression of the eyeball (oculomotor reflex) (Rothschild).

Higher grades of stenosis are always accompanied by diastolic murmurs. These always begin a short interval (0.08 to 0.09 second) after the second sound, *i. e.*, during the rapid inflow phase of the ventricle. They may be limited to mid-diastole or extend throughout diastole and thus merge with the presystolic murmur, as is well brought out in graphic records (Fig. 114). According to Lewis, the duration of the murmur is determined by the degree of stenosis. If this is slight and the rhythm regular, a presystolic murmur alone is present. If the stenosis is moderate, an early diastolic murmur separated from the next presystolic murmur also occurs, due to the inrush of blood into the relaxed ventricle. If stenosis is extreme, and especially if the heart is rapid, the entire period of diastole is filled with murmurs which pass into the period of presystole. In still more advanced cases, or, better expressed, in cases with marked "back-pressure effects," a diastolic or Graham Steell murmur may be heard over the pulmonary area, or a diastolic murmur may also be present over the tricuspid area, indicating relative insufficiency of the tricuspid valve. Systolic apical murmurs, such as are shown in Figs. 114 and 115, are frequently heard when regurgitation is associated with stenosis.

In all cases of long standing the left auricle and right ventricle hypertrophy, while the right auricle may also be dilated. Consequently, percussion shows a slight increase in cardiac dulness to the left, especially upward. In roentgen-ray plates and orthodiagrams the heart shadow resembles an oval with a vertical axis (Fig. 180). The enlarged left auricle is prominent on the left margin and in severe cases the pulmonary shadow bulges, giving the entire left border a step-like contour.

The electrocardiogram shows a prominent and often notched P wave (*cf.* Fig. 179 and Fig. 190, *A*, Lead II), and the initial complex is often inverted in Lead I (Fig. 190, *A*). Cases are found, however, where R_{III} is inverted.

The characteristic signs revealed by palpation and auscultation change when compensation falls. When auricular contraction becomes

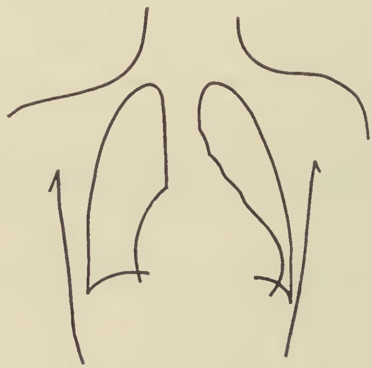

FIG. 180.—Mitral stenosis after prolonged loss of compensation. (Claytor and Merrill.)

weak, the presystolic murmur and thrill may disappear and the systolic shock alone remains. When auricular fibrillation supervenes and auricular contraction is absent, the presystolic murmur, strictly speaking, disappears (Mackenzie), or, better stated, perhaps, no murmur precedes the first heart sound when the rest of diastole is free from murmurs (Lewis). Diastolic murmurs alone are present during a portion of or throughout diastole. Owing to the varying length of diastole, the character of these murmurs changes from beat to beat (*cf.* Fig. 115). The shorter cycles may be filled with murmurs, while in long cycles they often occur only in the early portion. These murmurs are distinguished from the diastolic murmurs, due to aortic insufficiency by their slower frequency (lower pitch) and the fact that a short interval exists between the second sound and the murmur in mitral stenosis (Lewis). (*cf.* also page 329.)

When auricular fibrillation develops, the arterial pulse is extremely

irregular and the beats vary in amplitude. The temporal changes of the venous pulse and electrocardiogram in this condition have been analyzed elsewhere.[1]

AORTIC STENOSIS.

Aortic stenosis may exist as a simple lesion when the cusps undergo atheromatous degeneration but retain sufficient flexibility to close during diastole. When the entire valves are involved in the sclerotic process, however, or their edges fused, a certain degree of insufficiency is associated with the stenosis. This combination is not uncommon (40 per cent, Hirschfelder).

Hemodynamics.—When a stenosis is produced in an artificial circulation model, definite dynamic disturbances are recognizable: The intraventricular pressure increases greatly during systole, the systolic

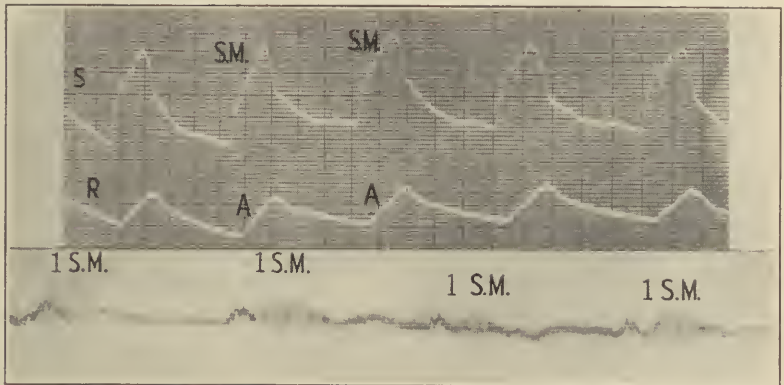

FIG. 181.—Subclavian pulse, *S*, and radial pulse, *S*, from case of aortic stenosis. Lower record, basal systolic murmurs from same, on more rapid paper showing variations with respiration. *S.M.*, systolic murmur; 1, first heart sound; *A*, anacrotic notch. (Courtesy of Dr. H. Feil.)

discharge is reduced, both systolic and diastolic pressures decrease, the pulse is smaller and shows a characteristic gradual rise (Fig. 174). The left auricular pressure increases and the volume of the auricles is augmented.

The results obtained in animal experiments are similar but modified by certain compensatory changes in the left ventricle (Luderitz, de Heer, Straub, Wiggers). In the first place, all investigators are in accord in the observation that a very considerable degree of stenosis is necessary before any pronounced changes in the circulation occur, although a systolic murmur may appear with relatively mild grades of stenosis. These may be heard and recorded not only over the aorta, but are transmitted to the right auricle and appear as still coarser vibrations on the aortic pulse tracings (*cf.* Fig. 181).

[1] *Cf.* page 481 *et seq.*

The sequence of dynamic events in severe stenosis may be considered as fairly well established as a result of the work of de Heer and Straub, which the author will essay to interpret in the light of unpublished experiments of his own. For a number of beats after the sudden production of a severe lesion, the results of artificial circulation experiments are duplicated. The systolic discharge of the ventricle decreases, the pulse pressure is reduced in the aorta and both systolic and diastolic pressures fall. The pressure curves change their contour, become more gradual in their rise and reach their summit more gradually. All evidence of a distinct primary peak is eliminated, but in place of this, an anacrotic hump occurs. The murmur vibrations now continue throughout ejection and a sharp incisura does not follow.

Within four or five beats physiological compensation on the part of the left ventricle takes place. As each systolic discharge is reduced, a systolic remainder is retained within the left ventricle and operates

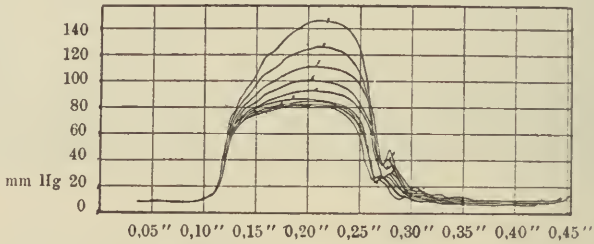

Fig. 182.—Intraventricular pressure curves in different degrees of aortic stenosis. (After de Heer.)

to increase the diastolic volume and initial tension. By virtue of this, the left ventricle, *a*, contracts more powerfully, elevating intraventricular pressure more rapidly and to a higher level (Fig. 182), and, *b*, appreciably lengthens its phase of systolic ejection. Both of these factors operate to restore the systolic discharge to normal, even when very considerable stenosis exists, as is shown by the amplitude of the volume curves and a study of the minute-volume output (Straub). As long as this compensation is maintained, any excess of blood which has accumulated in the left auricle is accommodated by its expansion and in the pulmonary venules. Consequently, neither the pulmonary arterial nor right ventricular pressures are affected (MacCallum, Straub). On the contrary, the maximum pressure in the right ventricle occasionally decreases (Straub). As soon as the left ventricle is not able to compensate in this manner, the systolic discharge decreases, the left ventricle and auricle dilate and pulmonary arterial pressure rises. This takes place in spite of a fall

in venous pressure and in spite of a reduced output from the right heart, hence it must be referred to a backing up of blood into the pulmonary circuit. To what extent this is due to the mechanical back-pressure effect of valve stenosis, and to what extent to dilatation and failure of the ventricle, have not been clearly separated.

Clinical Manifestations.—The earliest subjective symptoms are probably those arising from increased intraventricular tension and, perhaps, the impeded blood flow through the heart. They consist of a sense of constriction, substernal pain or anginal attacks, at first recurring only after excitement or exercise, but later being present without apparent exciting cause. Later in the course of the disease, when the right ventricle dilates, symptoms due to pulmonary engorgement and often tricuspid insufficiency supervene. Upon inspection, the apex-beat may not be forcible or there may be a slow, heaving impulse. The dulness is enlarged to the left and downward. Orthodiagrams show an enlargement of the heart shadow to the left. The lower portion gives the appearance of a horizontal oval, above which the shadows of the pulmonary artery and aorta are visible. The shadow, though smaller, resembles, in shape, that of aortic insufficiency. The enlargement is evidently due to hypertrophy of the left ventricle. In confirmation of this conclusion it is found that the R wave of the electrocardiogram is directed down in Lead III.[1]

Palpation often discovers an intense systolic thrill over the aortic region and a loud, rough, systolic murmur is also heard here. It is transmitted upward to the large vessels and may be registered from the lower neck. On registration, it consists of a series of irregular vibrations, occurring at the rate of about eighty per second, and beginning a short interval after the first sound (Fig. 181). (For further clinical details as to significance of basal systolic murmurs, *cf.* Addendum, Chapter XXV, page 576.)

The second sound is usually weak or may be entirely absent, while, if the valves fail to close it may be replaced by a diastolic murmur. The combination of aortic stenosis and insufficiency is very common, and then the circulatory changes are dominated by the insufficiency rather than the stenosis (Fig. 112).

The radial pulse is usually small and its rise is slow. The tracings sometimes show an anacrotic limb and occasionally a pulse with a typical slow rise. A good example is shown in Fig. 181. The combination of a systolic murmur over the aortic area and a palpable thrill alone are not sufficient to make a diagnosis of aortic stenosis, however, for such murmurs occur frequently and under a variety of conditions (*e. g.*, anemia, arteriosclerosis, etc.). Signs of left ventricular enlargement or deformation of the pulse curves should, therefore, be sought for in order to make the diagnosis quite clear.

[1] *Cf.* Fig. 190, *B.*

AORTIC INSUFFICIENCY.

Hemodynamics.—Since Corrigan, in 1832, first described and gave a logical explanation of the collapsing pulse frequently associated with aortic insufficiency, clinicians and physiologists alike have attempted to interpret the circulatory dynamics of this condition. Many of these interpretations consist merely of assumptions which conveniently explain the clinical findings; many of the experimental results also were derived by the use of apparatus inadequate for the demands and have served only to confuse the subject. It is, therefore, necessary to utilize the data at our command with great caution and discretion.

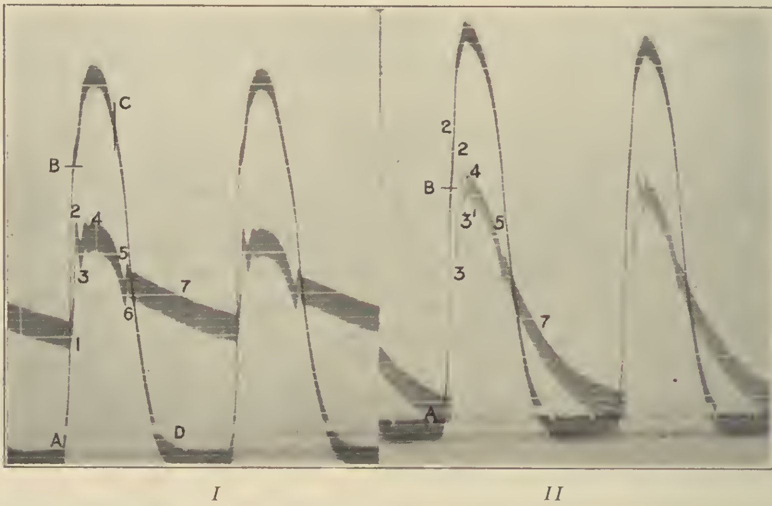

Fig. 183.—The subclavian and intraventricular pressure curves. *I*, normal; *II*, after aortic insufficiency. (Description in text.)

The dynamic effects of aortic regurgitation have been analyzed both in artificial circulation apparatus experiments (Marey, Moritz) and in animal experiments (Cohnheim, Rosenbach, Goddard, de Jager, Kornfeld, Stewart, MacCallum, Zollinger, Wiggers). It can readily be shown on an artificial circulation apparatus that the production of an aortic insufficiency causes a fall of diastolic pressure in the artery, while the systolic pressure either falls slightly or remains unchanged. The maximum pressure within the ventricle also falls slightly, but the diastolic pressure rises just before the next systole, although some discrepancies occur that can probably be attributed to experimental technic. Animal experiments have also shown that, after the production of a lesion the systolic pressure remains unchanged or falls slightly, while the diastolic and, consequently, the mean

pressures fall greatly (Kornfeld, MacCallum, Stewart). Whenever these changes occur, the pressure curve in the arteries and also the pulse alters its contour, in that the amplitude becomes greater and the descending limb more rapid in its fall (*cf.* Fig. 183). This change has usually been attributed to the fact that a considerable quantity of blood regurgitates into the ventricle during diastole, causing an augmented amount to be thrown out during the next systole. This suggestion was supported by the results of Kornfeld, who found that the left auricular pressure often rose after the lesion while the systemic pressure fell. Stewart, however, pointed out that this could not be the correct explanation for: (1) The rapid fall always occurs before the dicrotic notch, and, hence, during ventricular systole; (2) no appreciable regurgitation is shown in the volume curves of the heart. He, therefore, explained the rapid drop as the effect of a reflex vasodilatation, since, in the first place, this accounts for all the changes in pressure and pulse contour, and, in the second, the normal contour returns in spite of the lesion when the peripheral vessels are constricted during aortic insufficiency, as by aortic compression or the use of adrenalin. This conclusion, in turn, was not supported either by MacCallum or Hewlett, but neither of these investigators attempted to explain the results of Stewart.

Experiments reported by the author, in 1915, led to a somewhat different interpretation of the circulatory changes. In the first place, optical records of aortic pressure curves demonstrated clearly that *the chief drop of pressure responsible for the low diastolic pressure does occur in diastole and not, as Stewart was led to believe from inadequate pulse tracings, during systole.* This is well illustrated by comparing the two records of Fig. 183, where the incisura, marking the end of the systole, is indicated at 5 and the fall of diastolic pressure is shown at 7. Furthermore, on removing the insufficiency, the curves shown in *I* were reproduced within the time interval of a single beat. A careful consideration of these curves indicates that the large wave and the extreme fall of arterial pressure cannot possibly be due to a peripheral dilatation of vessels. These changes must be attributed to a back-leak of pressure into the ventricle, with or without an appreciable back-flow of blood.

The sequence of events are pictured as follows: Normally, the effective closure of the semilunar valves at the beginning of diastole not only prevents blood from regurgitating into the ventricle but permits the aortic pressure to decline slowly, while the intraventricular pressure (within 0.1 second) falls to a point where it is less than the intra-auricular pressure. This causes the *A–V* valves to open, and within 0.07 second more the ventricles are quite completely filled with blood from the auricles. Synchronous records of intra-aortic pressure (*cf.* Fig. 183) indicate clearly that the rapid diastolic decline of intraventricular pressure is not affected when the

aortic valves are rendered insufficient, and support Stewart's view that the ventricles, as is normally the case, are rapidly filled from the auricles. This occurs, as Stewart suggests, because blood flows through the larger mitral orifice under low pressure in preference to the small aortic opening under considerably greater pressure. When this natural filling is completed, little room is left for blood to enter by regurgitation from the aorta unless the ventricle is actually distended. Such distention, however, is so effectively resisted by the natural elasticity and tonus of the ventricle that only a very small volume of blood actually regurgitates. That this very small volume actually does flow back and that the amount depends upon the ventricular tonus cannot be denied, but *all experimental evidence contradicts the view so prevalently held by clinicians that a large portion of the systolic discharge flows back in each diastole.*

The essential dynamic disturbance, viz.: the collapsing pulse, is brought about, not by the volume of blood which regurgitates, but by the *regurgitation of pressure* during diastole. While the relatively small orifice in the insufficient valves, together with the rapid natural filling of the ventricle, prevents any considerable regurgitation of blood, it permits an equalization of pressure. This conception of the regurgitation of pressure without any appreciable back-flow of fluid may be clarified if we suppose a system consisting of two flasks, *A* and *B*, communicating by a rigid tubing and a stop-cock, to be completely filled with fluid. Let us suppose, further, that the stop-cock is closed and that the fluid in flask *A* is placed under a pressure of 5 mm. Hg. and that in flask *B* under the pressure of 150 mm. Hg. Upon opening the stop-cock, the pressure in the two flasks will become equal, that in flask *A* rising, that in flask *B* falling. It is obvious that since both flasks are already filled with an incompressible liquid, no transfer of liquid can take place. If both flasks were partially distensible, then a small transfer of fluid could take place.

The same events occur in the circulation. The pressure falls more rapidly within the aorta during diastole and to a lower level, thereby diminishing the diastolic pressure. In the ventricles, the initial pressure rises to a higher level. The rapid diastolic decrease in pressure within the central arteries causes a back flow of blood from the more peripheral arteries, as was actually demonstrated by Hewlett and Van Zwaluwenburg. This reflux of peripheral blood is largely accommodated in the large arteries, however, and is no index of actual regurgitation into the left ventricle.

The essential dynamic events responsible for the large pulse wave with each ejection are pictured as follows: The regurgitation of pressure, together with a small volume of blood, increases the diastolic volume and initial tension, as shown in the ventricular pressure curves of Fig. 183. This at once results in an increased systolic discharge. The increased systolic pressure summits in both aorta and

ventricle eventually results in the hypertrophy of the left heart. That these compensatory mechanisms are at once called into play is supported also by the results obtained on a heart-lung preparation by Schram in 1915 and by Straub in 1917. They were extended by the latter investigator particularly in regard to "back-pressure effects." The increased initial tension, occasioned during the first few beats after a lesion, slightly interferes with the auricular inflow for a few cycles and left auricular pressure consequently increases. Straub was not able to find, however, that either the right auricular or right ventricular pressures were affected and, consequently, we may conclude that "back-pressure effects" do not obtain in this lesion as long as compensation holds good.

Clinical Manifestations.—As long as a deficiency in cardiac action does not exist, the chief symptoms are probably the result of variations in arterial pressure. The arterial throbbing in the neck, chest and abdomen may be quite disturbing. Cerebral symptoms, headache, roaring in the ears, hallucinations of sight, hearing and smell are frequently present, but it seems never to have been shown whether they are the result of aortic insufficiency or of the same influence which is responsible for the insufficiency. The dull or anginoid pains over the heart and palpitation are probably due to the high pressures within the heart or aorta.

When physiological compensation fails and pulmonary congestion sets in, dyspnea, cough, cardiac asthma, etc., occur.

Patients with aortic insufficiency have a very characteristic appearance (aortic facies) which, upon casual inspection, suggests somewhat that of exophthalmic goiter. The complexion is pale and sallow, the cheeks are sunken, the pupils dilated and the palpebral fissures are wide. The peripheral vessels throb and a capillary pulse is visible in the finger nails.

Upon examination the apex-beat is displaced downward and to the left, sometimes extending to the fifth or sixth interspace in the anterior axillary line. A heaving impulse is usually visible. A pulsation of the aorta may be visible in the second right interspace.

Percussion shows, in cases of long standing, an immense increase in cardiac dulness, chiefly to the left and downward. The orthodiagram shows an outline which, while resembling that of stenosis, is very much larger (Fig. 184). The lower portion is a horizontal oval, while the entire figure is often described as shoe-shaped.

On palpation, one or more thrills may be felt, but are neither constant nor diagnostic. They may be systolic, diastolic or presystolic in time.

Auscultation of the cardiac base reveals a blowing, hissing or musical murmur early in diastole, closely following or replacing the second sound. Its greatest intensity is over the sternum opposite the third rib, or in the second right intercostal space. The first

sound is sometimes clear and of a snapping quality, but at others is replaced by a soft systolic murmur transmitted upward to the neck, where it may be recorded (Fig. 112). A presystolic murmur (Flint) is generally present at the apex. Its cause is still in doubt and will probably remain so until actual experiments supplant theoretical speculation. Flint ascribed it to a functional stenosis produced when the mitral valves are floated into position by the marked regurgitation.

The configuration of the recorded murmur varies with its auditory quality. The rougher blowing diastolic murmurs, which occur immediately after the second sound or replace it entirely, are often limited to early diastole (Fig. 112). They are composed of irregular decrescendo vibrations. A systolic murmur is frequently present, giving the murmur a to-and-fro character. The musical murmurs

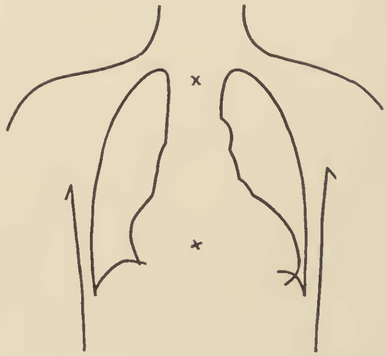

Fig. 184.—Orthodiagram of aortic insufficiency.

are entirely diastolic and usually extend through this entire phase (Lewis, Wilson and Jamieson). They are composed of uniform vibrations of large amplitude and resemble in many ways the regular vibrations of tuning-fork records (Fig. 113). The systolic murmur associated with this lesion is particularly well transmitted to the neck and recorded as a series of superimposed vibrations of the central pulse. It is still questionable whether this murmur is necessarily associated with some complicating stenosis or is due to a mechanical vibration of the blood currents.

In typical cases of aortic regurgitation, the radial pulse gives the palpating finger a sensation of sudden impact and rapid recoil or collapse. It has, therefore, been termed, since its description by Corrigan in 1832, as a "collapsing pulse" or a "water-hammer pulse." The collapsing type of pulse is associated, as Hewlett and Van Zwaluwenburg have demonstrated by means of the pulse-flow curve, with

an actual backward movement of blood from the arm, but whether this excess of blood is accommodated in the central arteries or actually regurgitates into the ventricle does not seem proven by their work. Physicians have repeatedly been impressed by the fact, however, that when a palpating finger receives the sensation of a collapsing pulse, the sphygmogram often fails to corroborate it. This has frequently been ascribed to the mechanical errors of the sphygmographs employed and with great reason, for it is often possible to obtain for the same patient entirely different pulse forms by using different instruments or by merely varying the pressures in the same instrument.

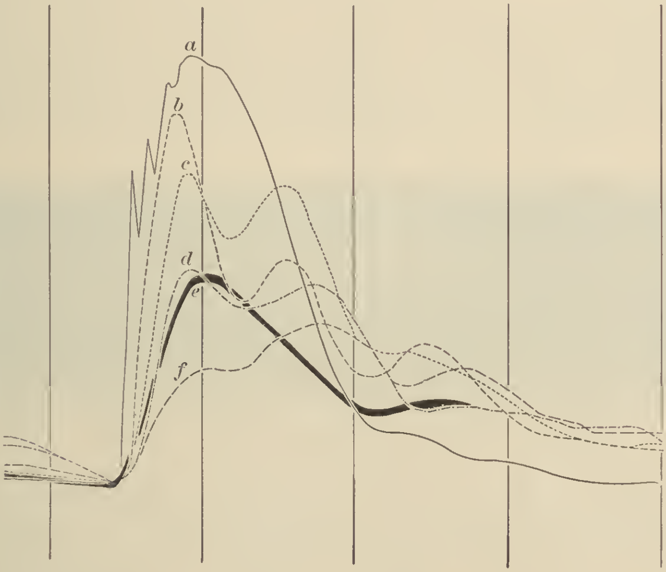

Fig. 185.—Transcribed curves of the radial pulse obtained in aortic disease. Curve in heavy lines, normal for comparison. Types, *a*, abrupt upstroke and thrill; *b*, abrupt upstroke and two peaks, the second smaller, *c–d*, pulsus bisferiens; *f*, anacrotic pulse. (After Feil and Gilder.)

The most comprehensive comparison of pulses obtained by optical sphygmograms, with the sensations felt on palpation, was made by Feil and Gilder. The chief variations of the radial forms, as compared to a normal pulse (drawn in heavy line) are shown in Fig. 185. They reached the following conclusions: The pulse as recorded graphically in aortic disease is exceedingly varied in form; the chief abnormal qualities it presents, and these may be displayed singly or in combination, are: (1) An unusually abrupt upstroke; (2) the presence of two prominent summits, which may be of equal or almost

equal height (bisferiens) or of which the first may be of distinctly less amplitude than the second (anacrotic); (3) the occasional presence of rapid oscillations on the upstroke or plateau, constituting a brief thrill. All of these qualities may be recognized, to a greater or less extent, by the palpating finger.

The impression of the water-hammer quality is caused by the abruptness with which the pulse pressure rises, and by this alone. The impression of the slow rise when the pulse is anacrotic is brought about by the great increase in the interval between the beginning of the upstroke and the actual summit (*i. e.*, formed in this instance by the second peak). The "bisferiens quality" is distinctly palpable when the summits are conspicuous and when they are separated by an interval of 0.129 second or more. Apart from the recognized quicker descent of pressure throughout the whole of the latter periods of the pulse cycle in aortic regurgitation, there appears to be no especially steep phase of descent which warrants the application of the term "collapse" to such pulses.

Fig. 186.—Erlanger sphygmomanometer tracing from case of aortic insufficiency. Diastolic reading about 58 degrees, systolic, indefinite.

Nearly all investigators find that the systolic pressure is normal or high (180 to 200) and the diastolic pressure low (60 to 30) (Huchard, Lian, Baj, Taussig and Cook, etc.). It is questionable whether it is necessary to call in the presence of arteriosclerosis to explain the high systolic pressure. With the Erlanger sphygmomanometer the change to smaller pulsations is usually sharp and distinct, permitting an accurate determination of diastolic pressure (Fig. 186). In employing the auscultatory method, it is necessary to take the fourth phase as the criterion, since the sounds do not entirely disappear at very low pressure in the bag. This plan corresponds quite accurately with the diminution in amplitude of oscillations. In determining systolic pressure in cases in which a collapsing pulse is present, difficulty is met in utilizing Erlanger's criterion, for the bases of waves do not separate as in a normal pulse (*cf.* Figs. 123, 124 and 186). The auscultatory or palpatory method must, therefore, be resorted to.

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CHAPTER XXV.

THE DYNAMIC CONSEQUENCES OF CHRONIC HEART DISEASE.

The changes in the circulation during chronic heart disease are predominantly determined by the functional behavior of the ventricular myocardium. It is, therefore, desirable to trace the logical processes through which the myocardium becomes deranged in its functions, to consider the factors of safety that are at once called into play, to analyze the additional compensatory mechanisms that are gradually developed and, finally, to attempt an answer as to why these mechanisms ultimately fail to accomplish the task for which they were developed.

Cardiac Strain and Fatigue.—Cardiac strain begins either when the normal ventricles are required to eject blood against a resistance higher than that to which they are normally accustomed, or, when, the resistance remaining the same, the inherent contractile function of the ventricles is impaired. In either case, there is a tendency for the ventricle, at once, to reduce its systolic discharge. This leaves a small systolic remainder which, when added to the volume entering in diastole, tends to increase both the diastolic volume and initial tension. Now, it is one of the well-established laws of the heart beat (Frank, Starling, Straub, Wiggers)[1] that, under these conditions, the irritability of the stretched and lengthened cardiac fibers is increased, and that, in consequence, they respond by increased contractions, thus restoring the systolic discharge to, and, in some cases, above normal.

In the case of a normal heart acting against the higher diastolic pressure, the pressure curves in the ventricles show a steeper rise and attain a higher pressure maximum, as is shown in Fig. 34. *In the case of the hypodynamic heart,* the pressure maximum has a tendency to decline, as shown in Fig. 187 (Curves 1, 2 and 3). The effect of increasing the initial pressure operates to restore the pressure maximum, approximately at least, to normal, as shown in case of Curve 3. In other words, "This means that the tired heart *must dilate* in order to carry on the same work as a normal heart." (Patterson, Piper and Starling.)

Obviously, there is a limit beyond which this adaptability of the heart no longer obtains. If the factors operating to increase the

[1] For references, *cf.* pages 105 *et seq.*

arterial resistance work too rapidly, or if the inherent contractile power fails too quickly, a second phase of cardiac strain begins. During this stage, as Bruns has shown in the frog's heart, the inherent contractility suffers. In the mammalian hearts, the intraventricular pressure curves do not mount so high and the isometric slope becomes more gradual, even though there is a progressive dilatation of the ventricle and an increased initial pressure (*cf.* Curves "190" and "240," Fig. 34). When this occurs, the second sounds may remain normal while the first sound vibrations become reduced in amplitude. Since the tonic contraction of the cardiac muscle and its elastic resist-

FIG. 187.—Transcribed curves of intraventricular pressure, showing the effect on the height and contour of the intraventricular pressure when initial pressures remain unaltered but inherent contractile power diminishes. 1, normal; 2 and 3, progressively decreasing contractile power; 3′, reaction of depressed heart to higher initial tension producing functional compensation.

ance are unable, for long periods of time, to resist the gradually increasing strain, the heart begins to weaken and finally gives way (Bruns). The ventricle then dilates enormously. This marks the onset of cardiac fatigue. Straub's experiments indicate that when this occurs the pressures in the left auricle become greatly elevated and the lungs markedly distended. The right ventricle, in consequence, is compelled to contract against a greater load; it then passes through the same phases of cardiac strain as the left. During the time that dilatation of the left ventricle is backing blood into the pulmonary circuit, the efficiently contracting right ventricle adds normal volumes

of blood to the pulmonary side; consequently, congestion cannot fail to supervene during the second stage of cardiac strain, while there may be no evidence of venous congestion.

Either one of two sequels must follow: The right ventricle may pass into the stage of dilatation, causing the venous pressure to rise and pulmonary pressure to fall, or new compensatory mechanisms may come into play which help to reëstablish normal relations.

Clinical Manifestations.—There are no signs that are pathognomonic of cardiac strain. As long as the myocardium is normal, the existence of accentuated sounds over the apex and aortic areas or an elevation of diastolic pressure may be taken to indicate that a strain of the left ventricle exists. The second sound is always accentuated, but in many instances the first sound is also affected. Neither of these signs exist, however, when a hypodynamic heart is overstrained, for in this case intraventricular and aortic pressures may be quite normal or even somewhat low. "Cardiac" pain is sometimes regarded as significant, but in view of more recent ideas it may be questioned whether this gives any direct indication of myocardial strain (*cf.* page 431). Similarly, an unstable rhythm or the incidence of ventricular premature systoles are too often associated with other conditions of the myocardium, to make them of definite diagnostic importance. Such individuals have a tendency to show breathlessness on exertion, but this, too, may point to other conditions than primary cardiac strain alone.

Tonus and Dilatation.—These terms are constantly employed by physiologists and clinicians alike, but often, it is feared, without a clear conception as to what they really imply. When the exposed heart appears large and distended during diastole, we often speak of a dilated heart or one having a low tonus. If, on the other hand, the diastolic volume is small, we are apt to speak of tonus as being high. As Patterson, Piper and Starling point out, the state of distention and tone are not necessarily related, "For the volume may be merely determined by the amount of blood entering from the veins." Henderson has shown that, as illustrated in Fig. 188, the diastolic volume of the heart is greater when the cycles are longer than when they are short. Furthermore, as shown in the lower series of Fig. 31, the diastolic volume at the same heart rate increases whenever the venous inflow is augmented. In each of these instances, the systolic volumes are normal, however, or at least approximately so. Such forms of dilatation may be called *physiological,* although they *may* occur in pathological conditions. As both the initial and maximal intraventricular tensions are augmented in this form of dilatation, Moritz has called it *tonogenic dilatation* (*i. e.,* due to increased tension).

Clinically, the term "dilatation" is applied to a condition in which the heart is dilated during diastole while the systolic discharge is

diminished; or, perhaps, more precisely stated, when the dilatation is not accompanied by a larger discharge. In other words, the heart is dilated during systole as well as diastole, a condition that is shown in the volume curves at E in Fig. 31. This type may be called a *pathological dilatation* (*myogenic dilatation* of Moritz).

Pathological dilatation is frequently attributed to a failure of cardiac tonus; the physiological type, to a passive distention in which tonus is normal. According to such conceptions, Patterson, Piper and Starling consider the term tonus "as synonymous with the physiological conditions or fitness of the muscle fibers and its measure is the energy set free per unit length of muscle fiber at each contraction of the heart. A heart with good tonus will carry on a large circulation and nearly empty itself at each contraction; a heart with defective tonus can eject the same systolic volumes only when its fibers are lengthened." This is also essentially the conception formulated by Moritz.

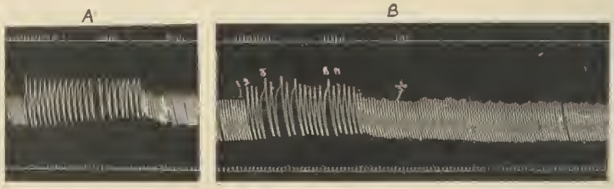


FIG. 188.—Two segments of drum records illustrating two types of effects after vagus stimulation. Systole, downstroke. *A*, diastolic distention with gradual tendency of heart to empty less completely during systole, attributed to impaired coronary blood flow; *B*, diastolic distention with complete systolic emptying, occurring when coronary supply is adequate. (After Wiggers and Katz.)

While this expresses the end-effects of tonus changes and relates the importance of tonus to cardiac efficiency very well, it does not clearly define the nature of tonus itself, nor does it analyze the mechanisms through which tonus governs cardiac efficiency. To physiologists the term "tonus" has come to signify a sort of a sustained partial contraction of muscle tissue, by virtue of which the muscle fibers resist stretching more than they would by virtue of the inherent elasticity alone. According to this conception, the ventricular varies directly as the volume-elasticity coefficient of the relaxed heart, *i. e.*, as the ratio of the pressure increase to the volume increase $\left(\frac{\triangle p}{\triangle v}\right)$.

This relation may be studied after the fashion schematically illustrated in Fig. 41. Let us suppose that, in such a preparation, sufficient fluid is admitted into the ventricle to raise the intraventricular pressure by eight equal increments. The volume changes corresponding to each of, say eight, such pressure elevations may then be plotted in step-like fashion. Comparison of the pressure changes in

the ventricles under varying conditions of tonus make it quite obvious that, when tonus is low, a much greater increase in volume accompanies a given pressure increase than when tonus is high; or, stated in the reverse, the same volume change is associated with a much greater pressure change when tonus is high than when it is low.

We may now again examine into the reasons why a heart with deficient tonus is less effective than the normal. Two hearts, distended to equal volumes, would have equal initial lengths. If this is the dominant or only factor determining the power of the heart to respond, we can only assign the decreased working capacity to an impairment of the muscular irritability itself. Such is apparently the conception of Starling and his associates. If, however, initial tension is primarily concerned in determining the working capacity of the heart, then the *reduced working capacity of the ventricle during atonia may be accounted for by the fact that, at equivalent initial volumes, the initial pressure is lower in the atonic than in the normal heart.*

The factors which may modify the cardiac tonus have not all been definitely established on an experimental basis. Thus, from the experiments of Socin it could not be definitely ascertained whether in cardiac depression from chloroform, tonus was also reduced. Bruns, however, was able to show definitely that tonus in the frog's ventricle is reduced when, for long periods of time, the heart is made to beat at a very rapid rate or compelled to work against increased resistance. According to Hering, the possibility that the tonus may be altered through nervous channels (*e. g., via* accelerator nerves) must also be considered.

Cardiac Insufficiency.—Cardiac insufficiency may be said to occur when the heart fails to discharge as much blood as it receives. From a dynamic aspect, *insufficiency occurs as soon as the maximum level of intraventricular pressure and the steepness of the isometric rise no longer increase with a rise of the initial tension in the ventricle* (Fig. 34). When this happens, the systemic pressures fall and the heart dilates because the systolic discharge is so greatly reduced. *Dilatation* and cardiac insufficiency have, therefore, become almost synonymous words. *Dilatation may accompany cardiac insufficiency* when the elastic resistance of the myocardium is overcome by the higher initial intraventricular pressure and the ventricle is *passively distended.* Dilatation, however, also occurs when the tonus diminishes, using the word *tonus* in its restricted sense, that is, a partial but sustained state of muscular contraction. *It is probably a cause rather than an accompaniment of cardiac insufficiency,* for, in such a case, the maximal efficiency for any need is not reduced primarily by a defect of the contraction power. On the contrary, it occurs because the lower tonus accommodates more fluid without increasing the initial tension and so fails to supply the conditions necessary for a stronger beat to expel the blood.

On the other hand, the heart may become inefficient from too high a state of tonus, for then the capacity is so reduced that the output per beat is diminished and the maximum intraventricular pressure becomes lower. It is clear, then, that insufficiency of the heart may be due to several causes and is not necessarily synonymous with dilatation or loss of tonus.

It is often difficult to determine which condition predominates when a dilatation is present. The relative rôles played by incomplete contraction and failure of tonus must be considered as not established. As older clinicians held largely to the idea of passive dilatation, so the recent tendency has been to give to tonus the entire responsibility. It may be true that the failure of tonus seems alone to account for the condition (Mackenzie) in certain cases, but it is not necessary to assume that all cases are concerned with such a failure. The whole question deserves a careful reinvestigation.

Clinical Manifestations of Dilatation and Cardiac Insufficiency.—Physiological increase in the diastolic volume of the heart, as we have seen, is a common occurrence; indeed, it represents the normal mechanisms by means of which the heart meets the greater demands of all the ordinary and more strenuous activities of every-day life. Except during severe exercise, such dilatation gives rise to few symptoms and signs. The myogenic form, presumably involving a reduction of tonus, presents more definite clinical pictures, however. The recognition of pathological dilatation and accompanying cardiac insufficiency depends—especially in the earlier phases—less upon the physical signs than upon the symptoms produced by an inadequate circulation.

Symptoms Referable to Inadequate Arterial Pressure.—With the reduction in the cardiac discharge, the arterial pressures would fall considerably were this not offset, as before pointed out, by compensatory vasoconstriction. Such vasoconstriction, however, reduces the capillary blood flow, and the inability to increase it properly during exercise is, probably, primarily responsible for the muscular weakness and fatigue. As the heart fails more and more, arterial pressures in the central arteries are inadequate to force a sufficient supply through the brain arteries. The resulting cerebral anemia is one of the causes of dyspnea and leads to fainting or syncope.

Symptoms Referable to Pulmonary Engorgement.—An engorgement of the pulmonary arterioles and capillaries not only slows the blood current, but causes an encroachment upon the alveolar spaces, thereby diminishing their air content. The "vital capacity" is, therefore, a valuable adjunct in diagnosis and prognosis (Peabody). This is directly responsible for oppressive thoracic sensations and is an indirect contributing cause of dyspnea. If engorgement becomes extreme, smaller pulmonary vessels may rupture or, as a terminal event, pulmonary edema may supervene.

Symptoms Referable to Venous Engorgement.—During cardiac insufficiency, blood stagnates not only in the right auricle and large veins, but a considerable portion is stored in the liver as well. This condition is readily recognized by the distended neck veins and the large, tender liver. The increased venous pressure spreads to the peripheral parts, acting not only to dilate the peripheral vessels, but also to retard the capillary flow. The increased capillary pressure results in an exemia, or filtration of fluid into the capillary spaces, which is responsible for the edema and ascites, on the one hand, and the concentration of blood evidenced by polycythemia, on the other. The slowed capillary stream permits an unusual reduction of the oxyhemoglobin and is the direct cause of the cyanosis in the mucous membranes, face, cheek and feet.

Symptoms on the Part of the Heart.—Dilatation, especially when acute, is frequently associated either with cardiac pain radiating to the shoulders and down the arm or with a sense of weight or oppression over the heart, due, it is supposed, to the greatly distended condition of the heart both during its systole and diastole.

Physical examination may reveal a diffuse and feeble apex-beat displaced to the left of the nipple line and an increased area of cardiac dulness, both to the right and left. The heart sounds may be feeble or replaced by soft murmurs. Evidence of venous engorgement may be present in the veins of the neck. In many instances, however, the symptoms of insufficiency may be present when physical examination can detect nothing that will add to the diagnosis.

The Reserve Power of the Heart or its Dynamic Factor of Safety.—It is well recognized that the ventricle does not utilize all its available energy during any ordinary contraction, but that a factor of safety exists which is commonly referred to as its *reserve power*. By this term is understood the potential energy which the ventricles are capable of developing, over and above (*a*) that required to overcome the aortic pressure resistance, plus (*b*) that required for the systolic elevation of pressure and the onward movement of blood. As the latter factor is small, however (*cf.* page 122), it may, for our purpose, be left out of consideration, and we may say that *the reserve power is expressed by the differences between intraventricular pressure curves, which results when the muscle contracts, as normally, in an after-loaded fashion and when it contracts isometrically, i. e., without change in volume.* Thus, if in Fig. 189, *I*, the curve A, B, C represents a normal intraventricular pressure curve, and A, B, C_2 the corresponding isometric contraction curve, then the pressure-difference between C and C_2 may be used as a measure of its reserve power *at that particular initial pressure.* If, for any reason, aortic resistance is augmented, so that the pressure curve is elevated higher, *i. e.*, A, B, C_1, then it is obvious that the reserve power, $C_1 C_2$, is decreased. It is, of course, also possible that it may be entirely abolished.

Such events rarely happen, however, in the normal heart, because the initial ventricular volume and initial tension simultaneously increase, as we have already noted. Now, this has the effect, within certain limits, of increasing reserve power, so that it not only remains an equal distance above the pressure maximum but may actually increase. This can be brought out in excellent fashion by graphic plots first worked from experiments on the frog's heart by Frank and subsequently adapted to the mammalian heart by Patterson, Piper and Starling. If, as in Fig. 189, *II*, we plot the volume-pressure relations of the relaxed ventricle, *i. e.*, the volume-distensibility

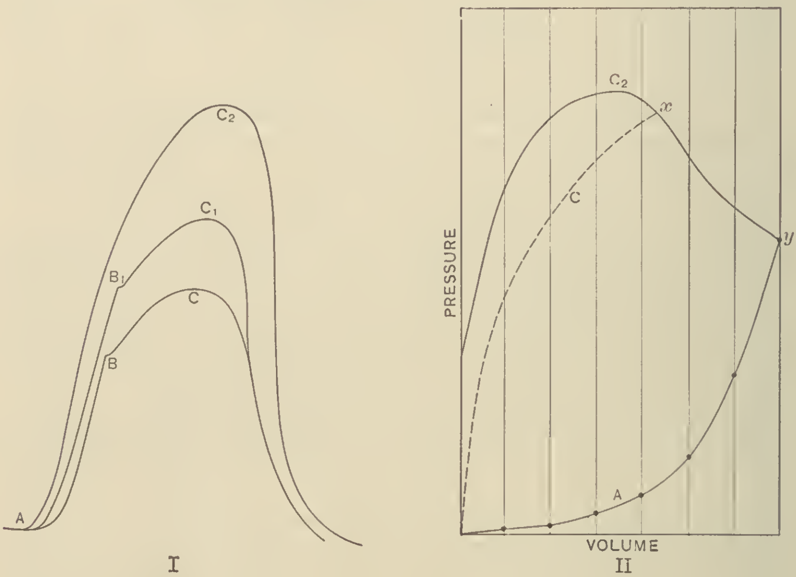


FIG. 189.—*I*, diagram showing differences in pressures when ventricle contracts in after-loaded fashion (*A*, *B*, *C* and *A*, B_1, C_1) and when it contracts isometrically, *A* C_2-*C* C_2 and C_1 C_2 represent reserve margin. *II*, plot of pressure-volume relations of the heart. *A*, during relaxed condition or diastole; *C*, when contracting after-loaded, C_2, during isometric contraction. Further description in text.

curve (obtained as described on page 120), in a lower record, *A*, and determine similarly the volume-pressure relations for similar points during the maximal isometric contraction, a curve, C_2, is, obtained. Finally, the volume-pressure relations, during maximal contraction under after-loaded conditions, may also be plotted on such coördinate paper, *C*. The vertical distances between *C* and C_2 then represents the reserve power at any initial pressure, and it is obvious that the closer the curve *C* lies to C_2 the less the reserve power at any state of diastolic distention. There comes a time when ventricular dilatation is so great that (as at *x*) the normal heart has no reserve power

left and, still later, it is conceivable, though not practically possible, that the initial volume and tension become so great that no further isometric contraction is possible at all, as at y.

When the myocardium becomes depressed, the time when no reserve power exists (*i. e.*, when curves C and C_2 meet) may become considerably advanced, so that at a relatively lower ventricular pressure the reserve power is absent. Experimentally, it is not possible in the mammalian heart to thus compare the auxotonic and isometric contraction curves. It is probable, however, that the reserve power is indicated at the point where consecutive increases in initial volume and tension no longer cause an increase in the pressure maximum and systolic discharge, but, as shown in Fig. 34, are accompanied by a decreased pressure maximum and a reduced discharge.

The Clinical Evaluation of Reserve Power.—We have as yet no direct method by which the criteria of reserve power, above discussed, may be even approximately estimated clinically. Fortunately, however, use may be made of this valuable conception in an indirect way, and one involving no apparatus of any kind. In everyday life the reserve power is latent when the body is at rest; but called into use, whenever physical effort is made. In fact, it is the means by which the increasing demands for blood during exercise of ordinary grades are met so that physical exertion is carried out without distressing symptoms. As soon, however, as physical exertion is carried to the point where the increased demand for blood cannot be met by increasing volumes of systolic discharge, the point is reached where initial volume and initial pressures are no longer capable of increasing the maximal pressure and systolic discharge. In other words, the reserve power as above defined is exhausted. Consequently, when this point is reached, certain symptoms, probably first recognized by Mackenzie as defining the field of cardiac response, supervene. Chief among them are sensations of breathlessness, suffocation or oppression across the chest and the consciousness of disagreeable action of the heart (Mackenzie). While these are symptoms that everyone with a normal heart has probably at one time or another experienced after violent exercise, it is the too ready occurrence of such signs which indicates a lower margin of cardiac reserve. Thus, when a patient presents a history of being unable to accomplish such physical tasks as he previously performed with ease, it may be taken as an indication that the reserve power is decreased, whether the heart is normal in size or hypertrophied. When the reserve power becomes very low, the patient may still be quite comfortable at rest, but is incapable then of performing even the most ordinary of physical exertions, *e. g.*, as walking on level ground.

Hypertrophy and Hypertrophic Compensation.—Whenever the mechanical work of the heart is permanently increased, and it is

continually required to work nearer its reserve limit, the metabolism of the muscle cells is so affected that they increase in size or hypertrophy. This involves not only an increase in the thickness of sarcoplasm, but also an increase in the number of muscle fibrils. The enlargement may affect the entire heart, but naturally occurs predominantly in that ventricle which is called upon to bear the brunt of the excess work. Thus, the left ventricle may be hypertrophied alone, or predominantly: (*a*) During lesions of the aortic valves; (*b*) in mitral regurgitation; (*c*) as a result of high blood-pressure, associated with general arteriosclerosis or renal disease; (*d*) after continued strenuous exercise or work. Similarly, hypertrophy of the right ventricle may occur alone, or predominantly: (*a*) In mitral stenosis; (*b*) in pulmonary valvular lesions; (*c*) in all conditions in which decompensation of the left heart has begun and the normal pulmonary resistance has increased. Often, however, hypertrophy appears to develop in the ventricle opposite to the one primarily affected by the valvular lesion, or when cardiac work is apparently not increased. Consequently, it is necessary to analyze the physiological coefficients responsible for hypertrophy and attempt, if possible, to explain the different forms on a common basis. This requires an analysis of the factors underlying augmented muscular activity.

In the first place, experimental and clinico-pathological results indicate that *increased work per minute* when unassociated with increased work per beat does not cause cardiac hypertrophy. When hypertrophy results from increased work per beat, it is conceivable that the stimulus to growth may reside: (*a*) In the greater shortening or greater tension developed in the individual muscle fibers during the process of contraction; or (*b*) in the increased length and initial tension to which the muscle fibers are subjected. While the literature that has grown around this phase of the question tends to leave the reviewer in a hopeless state of indecision, surveys of the subject, so well given in articles compiled by Grober, Thorel, Moritz, Hasebrock, Weizsäcker, etc., point toward the conclusion that probably increased dilatation and increased initial tension are the fundamental factors concerned (Fick, v. Frey, Horvath, Hasebroek). This interpretation necessitates the assumption *that a dilatation of the heart and increased length of muscle fibers are the sine qua non in cardiac hypertrophy.* Such dilatation may be of the physiological variety, *i. e.*, caused by increased tension (tonogenic dilatation of Moritz), or it may be due to a decrease in muscle tone (myogenic dilatation of Moritz). According to this conception, it is also possible to explain such types of hypertrophy as result when muscle effort is not as great as normal, *e. g.*, in myocarditis, toxic depression, etc. In other words, it has been suggested that it is not so much the absolute increase in muscle work which the ventricle is called upon to perform, as it is the nearness with which the muscle continually works to its reserve

limit. Thus, a weakened and dilated heart carrying out normal function is prone to hypertrophy under conditions which do not affect a normal heart.

The idea that a dilatation of the ventricle is a necessary prelude to the hypertrophy appears, on superficial examination, to clash with the pathological finding that dilatation may or may not be associated with hypertrophy. Such, however, is not the case. It should be borne in mind that it is not possible to gauge dilatation, as the term is used physiologically by postmortem examination, unless it is of tremendous degree and of the myogenic or pathological type. Physiological or so-called tonogenic dilatation can only be studied in the living heart.

Increase in diastolic volume and initial tension leading to hypertrophy of either the right or left ventricle is due to incomplete emptying against augmented resistance, as a result of which the ventricles dilate somewhat. A similar increase in diastolic volume may occur in other ways, however, *e. g.*, when a larger volume of blood is returned to the heart, as during exercise, in plethora, etc., or in the dynamic changes incident to mitral or tricuspid insufficiency (*cf.* page 536). In all of these cases, there may be no augmented resistance against which blood must be pumped. Under such conditions, it is possible to explain hypertrophy on the basis of the same common factor, viz.: increased diastolic volume and initial length. Indeed, there is evidence that the right side of the heart hypertrophies more often as a result of increased venous return than it does in response to an increased pulmonary arterial resistance which is comparatively rare.

Finally, the question must be considered as to whether other factors, such as changes in the quality and quantity of the blood supply, influence of toxic or infectious agents, etc., may not in themselves supply the inherent stimulus for muscle growth. That these influences may profoundly affect myocardial efficiency cannot be doubted; that they are, in any way, directly concerned with the production of hypertrophy is not clearly established. One of the best established principles in metabolism is, that the rate of metabolism is incapable of being enhanced by increased blood supply. Consequently, it is not probable that increased coronary supply, much as it may add to the efficiency of the heart, is in any way the stimulus for the growth of the cardiac elements. As already intimated, these agents are so generally associated with disturbances in function which lead to increase in diastolic length, that it is difficult to prove that they are specifically concerned in causing hypertrophy. At present, therefore, they may be regarded as secondary and not quite directly concerned with the production of hypertrophy.

It is generally stated that the biological consequence of hypertrophy is that it is able to accomplish the same tasks as the unhyper-

trophied muscle, not only with less effort, but with less tendency to fatigue, when additional strain is placed upon it. In other words, a *physiological hypertrophic compensation* occurs with anatomical *hypertrophy*. This belief is based, to a considerable extent, upon the increased microscopical size of the muscles elements, and the general biological observation that larger skeletal muscles are able to perform more work without fatigue. Direct experimental evidence that this applies also to the hypertrophied cardiac muscle and that the hypertrophic compensation is any way comparable to the increase in bulk is, however, meagre. It apparently rests largely upon the observations of Hasenfeld and Romberg, who showed that animals with recent aortic insufficiency bear the strain of aortic compression less effectively than those animals in which the ventricles have had time to hypertrophy. Nor is the dynamic change in hypertrophic compensation as yet entirely clear. According to Straub, two possibilities exist: (1) The hypertrophied ventricle may work according to the same conditions as a compensating normal ventricle, *but* a reversal effect in the maximum pressure and systolic discharge (*cf.* page 562) occurs at a relatively higher initial pressure. In such events the reserve power, though augmented, is never equal to that in normal hearts. This view is supported by many clinicians (*cf.* Krehl). (2) The hypertrophied ventricle, during rest, may respond with normal intraventricular pressure maximum and normal discharge at lower initial tensions and with less diastolic dilatation than the normal, in which case the reserve power at all times would be approximately equal to normal and compensation in a true sense would exist.

Desirable as further experimental investigations are upon these questions, we must recognize the difficulty of carrying out adequately controlled experiments upon this subject.

It is quite generally recognized that, while cardiac hypertrophy is accompanied by increased function, it sooner or later fails to accomplish the task for which it was designed. So general is this consequence that many clinicians have adopted the slogan, "An hypertrophied ventricle is always a diseased ventricle." This is probably due to a number of facts, among which may be mentioned: (*a*) That it is frequently associated with myocardial degenerations, which serve, as time goes on, to depress the contractile function of the heart more and more. In consequence, the reserve power is again reduced to that of the unhypertrophied heart. (*b*) Furthermore, cardiac irregularities may supervene and so interfere with the dynamics of the circulation that the reserve margin developed during hypertrophy, for regularly beating hearts is no longer adequate.

Clinical Manifestations of Cardiac Hypertrophy.—Clinically, hypertrophy of the ventricle cannot always be reliably distinguished. An enlargement of the heart revealed by percussion or by the use

of the orthodiagraph may be due to dilatation alone. In fact, with the exception of the hypertrophy of aortic insufficiency or nephritic hypertension, it is questionable whether the increase in size is great enough to be detectable by percussion (Sahli). Certain signs are generally considered not only suggestive, but also indicative of the side involved. Thus, an increase in the deep and relative dulness to the right is usually attributed to right-sided hypertrophy. It may be recalled, however, that the orthodiagrams show the right border to be composed largely of right auricle. It is questionable, therefore, whether a dilatation of the right ventricle can be diagnosed upon such evidence alone. Mackenzie has pointed out that dilatation of the right ventricle pushes the dulness to the left with the apex displaced downward and outward much as in left-sided hypertrophy. The difficulty in distinguishing right- from left-sided hypertrophy by percussion is, therefore, great. Fluoroscopic examination and a study of the form of the orthodiagram in various lesions is sometimes of assistance (see page 406).

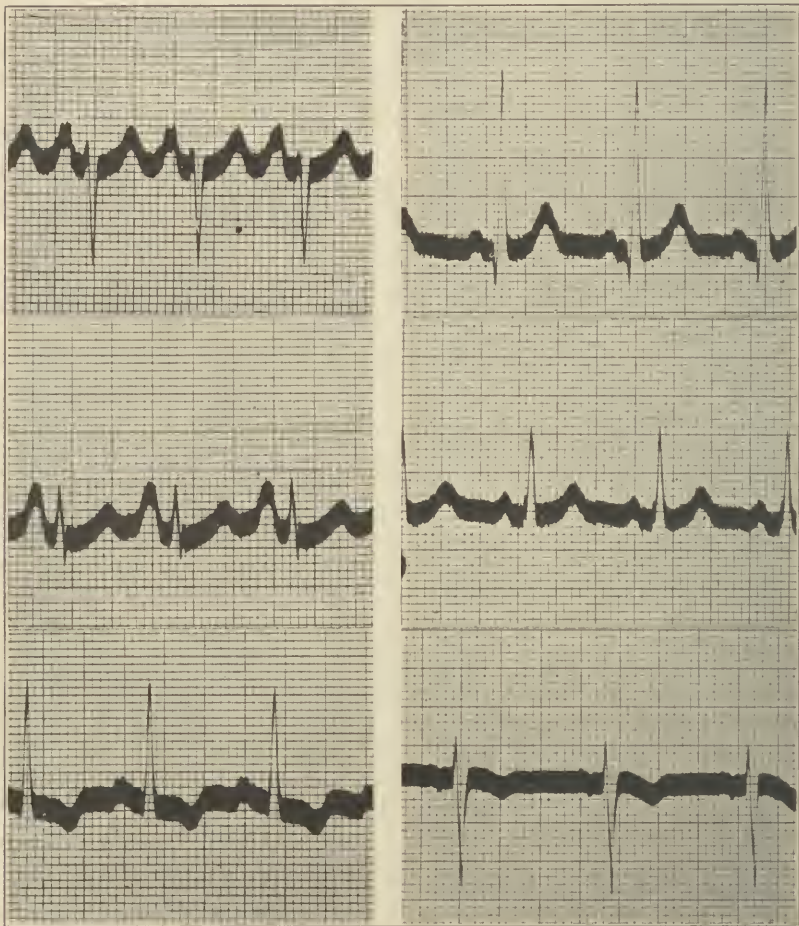
Frequently, however, roentgenographic studies are also fallacies, and do not determine which ventricle is chiefly involved (Carter, Greene, Lewis). Bardeen points out that, owing to the variable position of the heart within the chest, measurement of the cardiac border also fails to record accurately local changes. His evaluation studies show, however, that measurement of the cardiac area may be used both as an index of cardiac size as well as systolic volume. While the teleroentgenogram and orthodiogram gives us the best index to hypertrophy, they can throw little light on the relative degree to which different parts are affected (*cf.* also Chapter XIX, page 403).

Auscultation is considered of value in establishing the existence of hypertrophy. While an augmented second sound in the pulmonic or aortic area is presumably associated with a higher blood-pressure, it is by no means certain that this is associated with hypertrophy also. The presence of systolic murmurs reflected to the tricuspid and mitral regions, especially when they appear and disappear, may with more reason be regarded as a sign of dilatation, for when the muscular support is removed from the valve rings, a functional insufficiency probably results.

Probably the position of the apex-beat is the best clinical criterion that we have in locating the left border of the heart. Changes in the cardiac pulsations are said to be characteristic. Thus, a strong localized apex-beat associated with a large pulse is attributed to left ventricular hypertrophy; whereas, a diffuse apex-beat associated with a small pulse and epigastric pulsation favors right-sided hypertrophy. Little reliance can be placed upon a negative apex-beat during ventricular systole as a criterion of right-sided involvement. So much depends upon the placement of the tambour, upon the proper time allowance for transmission and upon the recording instru-

ments, that curves, such as presented by Mackenzie, for example, are far from convincing.

The value of the electrocardiogram in the diagnosis of hypertrophy has received considerable attention ever since the observation of



A B

Fig. 190.—Two sets of electrocardiogram of right and left-sided hypertrophy. *A*, hypertrophy of right ventricle following rheumatic endocarditis and mitral stenosis. Note large *P* wave in Lead II. *B*, hypertrophy of left ventricle, recent rheumatic endocarditis. Abscissæ, 1 div. = 0.04 second. (Courtesy of H. B. Williams.)

Einthoven that valvular lesions presumably accompanied by left- and right-sided hypertrophy, respectively, give electrocardiograms of distinctive type. Thus, as shown in Fig. 190, in mitral stenosis, presumably accompanied by right-sided enlargement, R_1 is directed

downward; whereas, in aortic insufficiency, accompanied by left-sided hypertrophy, R_{III} is directed downward. Einthoven, however, neither established its occurrence in the average range of clinical cases nor checked its reliability by postmortem studies. Neither did he give a complete explanation of the mechanism. As time went on, these gaps have been gradually filled. Lewis, in testing Einthoven's statement, observed certain discrepancies between the clinical diagnosis and electrocardiographic results, but noted that R_I was constantly negative in pulmonary stenosis and in the early years of infancy (*cf.* page 287). Lewis and, later, Cotton, and Herrmann and Wilson individually separated the ventricles by Müller's method. By comparing the relative weights of the ventricles thus established with electrocardiographic interpretations, it was shown that they checked markedly well, whereas ordinary clinical findings were substantiated in only about 70 per cent of cases.

From time to time, objections have been raised as to the validity of the so-called "electrocardiographic diagnosis of hypertrophy." Thus, Bridgman points out that, while American and English clinicians are inclined to accept such curves as diagnostic, many German clinicians have placed less reliance upon them. Bridgman himself makes a somewhat feeble attempt to throw the criterion into the discard, but, as Lewis points out, this is largely due to a misunderstanding between hypertrophy and preponderant hypertrophy. Waller has laid great stress on the fact that changes in the position of the heart give rise to curves that may readily be mistaken for hypertrophy. More recently, Fahr has postulated that the reversal of the initial complex obtained in such curves is occasioned by lengthening of one bundle branch, an interpretation which implies that reversal of R is associated with dilatation rather than with hypertrophy. Furthermore, Rothberger and Winterberg, among others, have shown that similar curves may be produced by bundle-branch block (*cf.* page 500). Aside from the fact that such curves usually present essential differences in contour, these lesions may frequently be ruled out, however, by other clinical data. In the most recent reinvestigation of the subject, Herrmann and Wilson conclude that the anticipated relation between relative weight of the two ventricles and the form of the electrocardiogram may be seriously affected by: (1) Changes in the position of the heart; (2) variations in the arrangement of the conducting system; (3) disturbances of intraventricular conduction. As the relative weight of the two ventricles is only one of the many factors determining the form of the ventricular complex, there is no definite relation between weight of one ventricle and ventricular complex unless one ventricle is greatly hypertrophied. Still more recently, Cohn has shown that, owing to abnormal positions of the heart, curves of preponderance of one ventricle may be derived from normal individuals and, *vice versa*,

that normal curves may be derived from individuals with enlarged hearts. The danger of drawing erroneous conclusions from the three regular leads is pointed out.

In spite of these objections, however, it may be said, with Carter and Greene, that, barring certain complicated cases, the electrocardiogram is the only satisfactory method we have by means of which relative preponderance of the ventricles may be interpreted.[1]

ADDENDUM.

The following instructions, taken from Circular 21, issued by the Office of the Surgeon-General for the information of medical officers in the examination of candidates for military service, may be profitably perpetuated as a guide to the interpretation of signs and symptoms.

PRINCIPLES OF INTERPRETATION.

The following principles are laid down for the guidance of examiners in their interpretation of abnormal signs and symptoms. In many cases the interpretation must be purely individual and based upon the cumulative evidence of a number of relatively slight deviations from the normal. It cannot be too strongly insisted on that, given a heart of normal size and responding normally to effort, any murmur that is heard should be considered accidental and insignificant unless it can be positively demonstrated that it is a mitral or aortic diastolic murmur. It should also be constantly borne in mind that the excitement of the examination may produce violent and rapid heart action, often associated with a transient systolic murmur, which may erroneously be attributed to the effects of exertion. They will usually disappear promptly in the recumbent posture, but the examiner must be shrewd to distinguish the excitable individuals and take measures to eliminate psychic influences from the test, so far as possible.

1. Hypertrophy and Dilatation of the Heart.

Impulse to the left of the nipple line or below the sixth rib and of heaving character is cause for rejection. Its cause, either valvular disease or hypertension in the majority of cases, should be sought for. It should not be made a primary diagnosis unless careful examination fails to reveal a cause.

Impulse within these limits, but definitely heaving, or relative cardiac dulness extending to the left of the nipple line, or more than 4 cm. to right of the median line in large, more than 3 cm. in small individuals, should lead to careful examination for valvular disease, high blood-pressure, emphysema or other cause. Unless such other cause can be found, the response to exercise shall be the guide. Those cases with normal response to exercise may be accepted for special service; (3) all others shall be rejected.

2. Valvular Diseases.

Cardiac murmurs are the most certain physical signs by which valvular disease may be recognized and its location determined, but murmurs are very frequent in the absence of valvular lesions and may occur in perfectly

[1] For articles dealing with indices for estimating the degree of left or right-sided phenomenon, *cf.* White and Bock (Am. Jour. Med. Sci., 1918, **156**, 17) and Carter and Greene (Arch. Int. Med., 1919, **24**, 638).

healthy hearts, especially under the influence of excitement and exertion. Such accidental murmurs are always systolic in time. The most frequent are as follows:

(*a*) Those heard at the apex on excitement, especially when recumbent.

(*b*) Those heard over the second and third left interspaces during expiration, disappearing during forced inspiration. These are particularly common in men with flexible chests who can produce extreme forced expiration and, under such circumstances, may be associated with definite thrill.

(*c*) Systolic accentuation of the respiratory murmur, especially on inspiration, heard near the apex or over the back.

None of the above shall be considered disqualifying for active service.

Other systolic murmurs unassociated with enlargement of the heart, alteration of the first sound, accentuation of the pulmonic second sound or abnormal response to exercise may also be considered as without significance, but should be noted.

Loud systolic murmurs, audible at the apex and in the left back, if associated with any enlargement of the heart, with snapping first sound, or accentuation of the pulmonic second sound, shall be cause for rejection. If unassociated with these other signs and the response to exercise be normal the recruit may be accepted for special service (3).

Systolic murmurs at the base, except as specified above, especially those heard in the second right intercostal space, require more careful scrutiny. They may be due to disease of the aortic valves. In this case they should be harsh, conveyed well into the neck, associated with an aortic diastolic murmur, with thrill, or with a marked enfeeblement of the aortic second sound. Any of these combinations shall disqualify. They are more often due to dilatation of the aorta, either syphilitic or arteriosclerotic. The other signs of dilatation should then be sought—increased dulness in the first and second interspaces to either side of the manubrium, pulsation in this area, and accentuation of the aortic second sound. In doubtful cases, Roentgen-ray examination and Wassermann test should be obtained. Where a slight systolic murmur in this situation is the only abnormal sign and the response to exercise normal, giving rise neither to breathlessness nor thoracic pain or distress, it shall not disqualify. Proved dilatation of the aortic arch, or syphilis of the aorta, shall be cause for rejection for active service, but if without symptoms shall not disqualify for special service (3). It shall be noted on the record. Systolic murmurs heard over the second and third left interspaces are almost always accidental and insignificant. When loud and harsh, heard over the upper left chest, front and back, or associated with thrill during quiet breathing, they may indicate congenital cardiac disease and shall disqualify.

All diastolic murmurs, at apex or base, including presystolic murmurs, shall be considered evidence of valvular disease and cause for rejection. The secondary signs should be sought for, viz.: Enlargement of one or both sides of the heart, alteration of the first or second sound, particularly a snapping first sound and accentuated pulmonic second sound in mitral disease, and the characteristic pulse of aortic insufficiency. In doubtful cases a definite history of rheumatic fever may be given weight. The exact diagnosis should be noted on the record.

3. Aneurysm and Dilatation of the Aortic Arch.

Aneurysm, wherever situated, shall disqualify.

Aneurysm of the thoracic aorta, unless large or placed near the anterior thoracic wall or giving rise to pressure symptoms, is difficult of detection. Simple dilatation of the aortic arch is a diagnosis which can rarely be made

positively from physical signs alone. Therefore, when pulsation above the base of the heart, diastolic shock, well-marked dulness laterally to the manubrium, with a ringing second sound or a systolic or diastolic murmur over the dull area, or tracheal tug, inequality of the pupils, difference in the two radial pulses, alteration of the voice or suspicious symptoms suggest the existence of aneurysm or dilatation, roentgen-ray examination and Wassermann test should be obtained. Any considerable dilatation of the aorta shall disqualify. Slight dilatation with a negative Wassermann reaction shall not disqualify, if it be the only impairment and unassociated with symptoms and abnormal response to exercise. Precordial or other anginal pain, which the examiner is convinced is real, may occur without dyspnea, and is significant.

4. Disturbances of Rate and Rhythm.

A persistent rate of 100 or over, when recumbent, should suggest the search for exophthalmic goiter, tuberculosis or other infection, which would constitute cause for rejection. Persistent rapid heart action, in the absence of proof of these, and unassociated with enlargement of the heart, may require study in hospital to determine its significance. A constant rate of 100 or more should disqualify. Temporary tachycardia on excitement is common. If extreme, the decision as to its significance must depend upon other findings, especially on the response to exercise. A reliable history of attacks of severe tachycardia in the past, with any breathlessness on exertion, should be reported to the camp surgeon with request for watching of the recruit during his training.

A persistent rate of 50 or under suggests heart-block, and this should be excluded by tracings. Heart-block shall disqualify. Slow rate with normal rhythm and normal response to exercise shall not disqualify. Complete irregularity of the pulse indicates auricular fibrillation and shall disqualify. It is not compatible with normal response to exercise.

Occasional dropped or premature beats, if the heart be of normal size and the response to exercise normal, are of no significance. Very frequent dropped or premature beats require reëxamination to determine if they are temporary. When persistent, but the only impairment, they should be reported to the camp surgeon, with request for watching of the recruit during his training.

The irregularity, which consists in a quickening of the rate during inspiration and slowing during expiration, is common in the young and is of no significance. It may be recognized most easily with the subject recumbent and breathing deeply.

5. Arteriosclerosis and Hypertension.

All subjects with thickened arteries, apparently tense pulse and accentuation of the aortic second sound, shall have their blood-pressures recorded when lying quietly, the systolic pressure by the palpatory and auscultatory, the diastolic by the auscultatory method. A systolic pressure of 200 mm. Hg. or over or a diastolic of 120 mm. Hg. or over shall disqualify. A systolic pressure persistently above 160 mm. or a diastolic above 100 mm. shall disqualify for active service; but if this be the only impairment, the recruit may be accepted for special service (3). The urine should always be tested for albumin in these cases.

Simple thickening of the arteries without high blood-pressure or enlargement of the heart and with normal response to exercise shall not disqualify.

6. Other Conditions.

Cases with unusual findings, not covered by these instructions, may be determined on the general principle that, if the heart be not enlarged and

its response to effort be normal, it shall not disqualify. If the response to effort be impaired, but the heart normal in every other respect, and if the subject has not been capable in the past of ordinary active exercise, he should be accepted for special service (3) or reported to the camp surgeon for watching during his training.

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CHAPTER XXVI.

CIRCULATORY FAILURE.

THE term "circulatory failure" characterizes any condition in which the arterial pressure and, consequently, the capillary blood stream are reduced to such an extent that, if long continued, the functions of normal organs are impaired and those of previously deranged organs are prevented from regaining their normal activity. Such failure may be a consequence of: (*a*) A deficient volume of circulating blood (oligemia); (*b*) obstruction in the pulmonary circulation (*e. g.*, embolism; (*c*) primary myocardial failure.

OLIGEMIA.

Oligemia is a condition in which the volume of circulating blood is diminished. It occurs acutely during a progressive hemorrhage and at times when water is rapidly abstracted from the blood by osmotic or secretory influences. The abstraction of water during serious diarrhea has long been recognized and its significance in severe diarrheas of infancy has recently received considerable recognition (Marriott). Rogers showed that in cholera 64 per cent of the blood serum may be lost. A concentration of blood has also been found in pneumonia (Sandelowsky), influenza (Underhill and Ringer) and in scarlet fever (Oppenheimer and Reiss). Such a concentration of blood and reduction in volume also accompany traumatic and wound shock (Sherrington and Coperan, Henderson, Keith, Gasser, Erlanger and Meek), and, according to many investigators, is largely responsible for the changes in the circulation in toxemic as well as traumatic shock.

Pathological Physiology.—When the volume of circulating blood is so far reduced that the various compensating mechanisms are unable to maintain a normal effective venous pressure in the right auricle, it usually happens that the effective pressure in the left auricle also falls. In consequence the output of the left heart diminishes and tends to lower the arterial pressure. Such a tendency usually prevails, although counteracted by a reflex peripheral constriction. Hence, both systolic and diastolic pressures are low, the pulse pressure is small and the product of heart rate and pulse pressure decreases.

The detailed changes that occur in the volume curves are shown in Fig. 191; the amplitude of the downstroke, indicating the systolic discharge, is smaller partly because the rate of diastolic filling is more

gradual (*cf.* lines *A*, *B* and *C*) and partly, also, because the velocity of ventricular ejection is decreased.

The characteristic pressure changes within the right ventricle are shown in Fig. 192: The initial pressure, *b*, progressively decreases with the diminished ventricular filling, the pressure maximum, *d*,

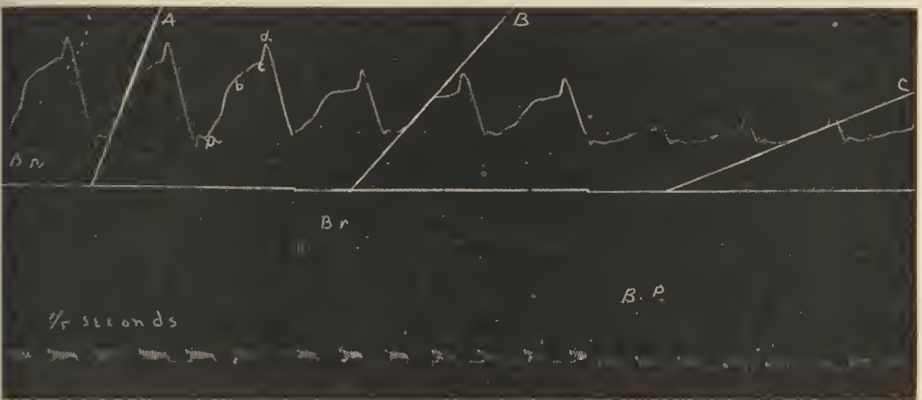

FIG. 191.—Ventricular volume curves, showing effect of diminishing the venous return on the rate of ventricular filling and systolic discharge. *A*, normal; *B*, after moderate hemorrhage; *C*, after severe hemorrhage.

becomes progressively lower, the gradient of the pressure rise during the isometric phase of the systole becomes more gradual, *b–c*, and the curve during the ejection phase presents a rounded summit rather than a plateau. Similar changes occur in the left ventricle.

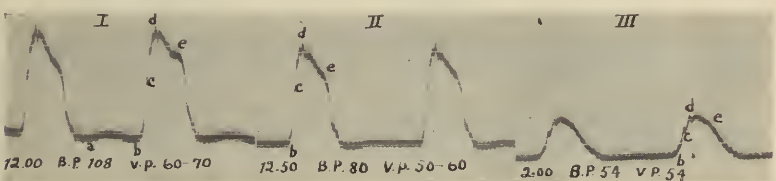

FIG. 192.—(Two-fifths actual size.) Segments of optical right intraventricular pressure curves in different stages of circulatory failure: *a*, *b*, auricular systole; *b–c*, isometric contraction phase; *c–e*, systolic ejection phase. *I*, normal before operation on abdomen; *II*, after exposure and manipulation of intestines (initial stage); *III*, late portion of progressive phase.

The characteristic changes in the contour of the aortic pressure curves are shown in Fig. 193: The amplitude becomes progressively smaller, all sharp vibrations and deflections characteristic of the normal central pulse disappear and the curve is transformed into one of smooth and rounded contour. The curve falls entirely during

systole[1] and becomes almost horizontal during diastole, indicating that practically no peripheral flow occurs during this phase. Calibrated records (Fig. 193) show that both systolic and diastolic press-

Fig. 193.—(Three-eighths actual size). Segments of optical arterial tracings taken during progressive failure of the circulation in shock. Numerals correspond to those in Fig. 194, so that relations to other events can be studied.

[1] *Cf.* Fig. 193, XV, etc.

ures fall, but the decrease in systolic pressure is the greater, making the pulse pressure smaller.

Clinical Manifestations.—Circulatory failure resulting from oligemia is recognizable by the following symptom-complex: A cold, moist skin; white, pale, grayish or slightly cyanotic appearance; great thirst and often vomiting. The respiration is usually rapid, but may be either deepened or shallow. Patients are first restless and very anxious but lapse gradually into a listless or apathetic state. Reactions to painful stimuli are reduced. The pulse is always rapid and feeble, the heart sounds are weak and body temperature is subnormal.

HEMORRHAGE.

Sequence of Events.— *The Initial Stage.*—The moment that an artery of considerable size ruptures, the total resistance against which blood is discharged is reduced; consequently, a fall in diastolic pressure results. The systolic pressure also decreases, though not to the same extent as the diastolic; hence, the pulse pressure increases. The amplitude of the pulse, which is determined by the pulse pressure, accordingly becomes larger and the shape of the peripheral pulse, which is determined by the low resistance, assumes the collapsing form.

While a smaller volume of blood is transferred from the arteries to the veins, neither the central venous pressure, the diastolic filling nor the systolic discharge of the ventricles is reduced during this stage (Wiggers, Meek and Eyster[1]). Several factors may account for this: (1) The reduced volume of blood returned from one region may be compensated by a luxus supply from another (Wiggers); (2) a dilution of blood from resorption of lymph may take place (Milroy); (3) blood may be withdrawn from the liver by a vasoconstriction (Krogh); (4) a general constriction of capillaries and venules may place more blood into circulation (Meek and Eyster). The duration of this stage, as well as the volume of blood that may be lost before the diastolic filling of the ventricles is affected, depends upon the rate of blood loss. In large hemorrhages it may last only a few minutes (Wiggers), and occurs when as little as 2.5 per cent of the original blood volume has been lost. On the other hand, as much as 15 per cent of the original blood volume may be very slowly withdrawn, without demonstrable changes in diastolic filling and ejection (Meek and Eyster).[1]

Stage of Decreased Ventricular Discharge.—When the compensating mechanisms are not able to keep pace with the withdrawal of blood, the circulating volume is reduced. The effective right auricular

[1] *Cf.* also Burton-Opitz (Jour. Am. Med. Assn., 1922, **78**, 1377).

pressure is then decreased, the volume curve of the ventricles diminishes in amplitude (Fig. 191), the fluoroscopic heart shadow becomes smaller, pulmonary arterial and left auricular pressures decrease, the systemic pressures fall rapidly, the pulse pressure becomes smaller and the volume of blood flowing through the organs is reduced (Gesell, Meyer, Seyderhelm and Wiggers).

This tendency for arterial pressures to fall rapidly as a result of oligemia is counteracted to a certain extent by a number of compensatory mechanisms. Even a small reduction in blood flow through the medulla causes: (*a*) An increase in depth and rate of respiration, which tends to favor the return of blood (pressor mechanism of respiration, Wiggers); (*b*) an inhibition of the vagus center (Fredericq, Hagen), causing an increased heart rate; (*c*) a stimulation of the vasomotor center (Sollmann and Pilcher), causing a constriction of peripheral bloodvessels. The latter not only produces an increased resistance and thereby raises the systemic pressure, but, by contracting the arterial system to more nearly fit the reduced blood volume, places a relatively larger volume of remaining blood into currency.

The purpose of these compensatory reactions is to keep the blood-pressure up so as to supply the vital organs, such as the brain and heart, with relatively more blood, even at the expense of a reduced blood flow to the other organs. It has been definitely shown that such vasoconstriction as supervenes during hemorrhage acts directly to cause a decreased flow of blood from the arteries to the capillaries, in spite of the fact that the viscosity of blood is reduced (Cope). It is obvious, therefore, that the medullary centers are, in a sense, the guardians of an adequate cerebral blood supply.

While these dynamic changes are taking place, a series of important chemical changes occur in the blood. The loss of red cells from the circulation, aided by the slower capillary circulation, leads to a decrease in the volume per cent of oxygen first in the venous blood (Doi) and, later, as the rate of O_2 absorption decreases (Schlomovitz), in the arterial blood as well. The CO_2 volumes are apparently not primarily affected (Henderson and Haggard). That this condition of anoxemia is also responsible for the reduction in alkali reserve cannot be questioned, but the precise mechanism is debatable. According to Henderson and Haggard, the lack of O_2 is solely responsible for the increase in respiratory activity, which causes a blowing off of CO_2 and a subsequent retirement of alkali reserve from the blood. According to other investigators, the reduced alkali reserve is due to the formation of organic acids (*e. g.*, lactic) as a result of impaired tissue oxidation.

Coincident with these changes, there is also a compensatory attempt to increase the blood volume by reabsorption of tissue fluids (Worm-Müller, Milroy, Gesell). Consequently, the viscosity of the blood

decreases (Burton-Opitz) and the percentage of red cells and hemoglobin is reduced (Dawson, Robertson and Bock).

The Mechanism of Hemorrhage Cessation.—Every hemorrhage, except one coming from a very large vessel, has a natural tendency to be checked long before the loss of blood becomes dangerous. The duration of bleeding depends not so much upon the size of the vessel wounded as on the facility with which an efficient clot forms over the opening. When blood is shed, it begins to coagulate on the tissues at a distance from the opening. Having formed a point of adhesion to the tissues, it is added to by accretion until it reaches and covers the wound. The factors which, aside from the coagulation time, determine the distance of the first clot formation and its development are, therefore, directly concerned with the duration of the hemorrhage. They may be enumerated as follows:

1. Other factors being equal, the pressure at the arterial opening determines the distance that the blood will be ejected before the force is sufficiently spent to permit the coagulum to form. A clot once formed is called upon to resist not the mean but the maximal pressure that exists in the artery.

2. The surface on which blood is shed determines the extent of its spread. Thus, the smooth surface upon which the intestinal and uterine vessels rupture compares unfavorably with the reticular lung parenchyma and subcutaneous connective tissue. So, also, the spread may be limited by an ulceration or an excavation.

3. The formation of clots may be retarded or prevented by muscular contractions of organs. The regular cardiac contractions, as a rule, absolutely prevent the formation of clots over wounds of the heart and forms the only serious element in such wounds. The rhythmic peristalsis of the stomach and intestines is very unfavorable to clot formation.

Events following the Cessation of Hemorrhage.—When hemorrhage terminates favorably by coagulation, the volume of blood returned to the right auricle increases with surprising rapidity. This is shown by fluoroscopic examination, by the ventricular volume curves, as well as by the increase in venous pressure quickly following the cessation of hemorrhage. An immediate increase is often due to the prompt rise of arterial pressure following clot formation or the application of a hemostat, but the slower increase after cessation of hemorrhage must be attributed to the rapid absorption of lymph to replete the blood volume. This dilution of the blood further decreases the number of red cells and diminishes the percentage of hemoglobin (Dawson), thus explaining the posthemorrhagic decrease in both for several days. Attention has been called to the fact that the fluid thus returned is apparently poor in alkali, for the alkali reserve continues to decrease after hemorrhage. This may, of course, be attributed also to the greater production of acid by the tissue or to a low blood CO_2

which is not able to recall the alkali to the blood (Henderson and Haggard).

In consequence of the better venous supply and greater output of both ventricles, the pulse pressure increases, for there is little alteration in the peripheral resistance and the increase in the volume-elasticity coefficient remains almost a negligible factor. Both systolic and diastolic pressures gradually rise, owing to the augmented cardiac output. The assumption is generally made that this posthemorrhagic increase in mean pressure is further assisted by an additional vasoconstriction; indeed, this is often quoted as a chief cause for the recovery of pressure. All experimental observations indicate, however, that vasoconstriction is a gradual process, starting while hemorrhage is still in progress and continuing after its cessation. Neither experiments nor *a priori* reasoning, however, warrant the assumption that a greater vasomotor reaction after hemorrhage is at all likely to occur, nor is such an assumption necessary to explain this posthemorrhagic increase.

The rise of arterial pressure, together with the continued dilution of the blood, gradually tends to increase the rate of flow both in the peripheral tissues and in the medulla. This results in a better oxygen supply of the tissues. The stimulation of the respiratory center gradually diminishes and the respirations become normal again. The heart continues rapid, however, and the peripheral vessels remain contracted until sufficient regeneration of the red blood cells has taken place to reëstablish normal conditions.

Events in the Terminal Stage.—If coagulation fails to occur, the time soon comes when the reduction in blood volume exceeds the possibilities of lymph absorption to such an extent that the mechanical function of the circulation cannot be efficiently carried out. The amplitude of cardiac contraction then decreases, largely because fluid is lacking to feed the pump.

In the last analysis, death, of course, is due to the extreme reduction of cellular oxygen, which results when arterial pressures are very low. Of all functions, however, respiration is the first to fail. The deep breathing progressively decreases and slow, shallow breathing supervenes. Finally, complete apnea broken only by an occasional deep gasp occurs. This is usually accompanied by a further decline in blood-pressure, for the "pressor effect" of respiration is entirely removed. Soon the heart-beats become slow, but of great amplitude and vigor, thus making a last and final attempt to elevate the pressure and restore an adequate blood supply to the medulla. This may be successful for a time, but finally fails for want of oxygen.

The final effects of anoxemia on the heart have recently been studied by Greene and Gilbert. They found that the post-crisis cardiac slowing is due to vagal stimulation. This may cause a complete inhibition of *S–A* rhythm and a transfer of the pacemaker to the

A–V node or even to a branch of the His bundle itself. Finally, as the vagus center too becomes depressed a more rapid ventricular rate is again established, with the S–A node assuming the role of pacemaker.

Clinical Manifestations.—From a clinical point of view, hemorrhages may be classified as *accessible* and *inaccessible*. In the former class belong external hemorrhages, as from the mouth, nose, throat, wounds, etc., and such *internal* hemorrhages as can be reached or inspected by special methods, namely, those from the uterus, urethra, bladder, rectum, etc. In the latter class may be listed such internal hemorrhages as intestinal, pulmonary, renal, cardiac and cerebral. In all of these forms, aside from the loss of blood and the dynamic changes in the circulation, the functions of all organs suffer in varying degree. The signs and symptoms, therefore, common to all forms of hemorrhage are due partly to changes in the circulation itself and partly to altered functions of various organs. In addition, there are often special symptoms resulting from an extreme interference with the function of the organ in which the hemorrhage occurs.

The *general symptoms* may be considered in four groups: (1) Those immediately following a hemorrhage; (2) those occurring during its progress; (3) those following cessation; (4) those preceding a fatal termination.

Immediately after the occurrence of an obscure, internal hemorrhage of moderate degree the patient may have few symptoms. If the hemorrhage is large, however, and the fall of arterial blood-pressure sudden, the attendant cerebral anemia gives rise to various cerebral phenomena. These may be: Nausea, vertigo or faintness, sensations of flashes of light, ringing in the ears, etc. The pulse is rapid and of large amplitude. The respirations are increased and the minute volume of air breathed considerably augmented.

As hemorrhage continues—the interval depending upon the amount of blood lost—other symptoms make their appearance. The skin and mucous membranes are pale and the body feels cold. These are partly attributable to the lower pressure, but partly also to an increased peripheral constriction, directing the blood flow internally. Muscular weakness now comes on, tremors appear and the voice is weaker. The breathing is increased in rate and depth, resulting in a condition long known as "air hunger," and a cold sweat appears. Meanwhile, the blood-pressure has fallen, the pulse has become small and increasingly rapid and the heart sounds, especially the second, have weakened. Blood examination shows a decrease in red cells and hemoglobin percentage, also a lessened specific gravity.

If the hemorrhage ceases at this stage, the symptoms may remain practically unaltered for a time, which makes it difficult to decide whether or not the hemorrhage is continuing. The pulse is still rapid with no discernible change in amplitude. Augmented respi-

rations may continue or they may become slower and more shallow, and it is impossible to determine whether this latter condition signifies recovery or that a fatal end is approaching. The hemoglobin and red cells continue to diminish for several days, due to the greater dilution of the blood by incoming tissue fluids. The pressure, however, begins a steady rise and the pulse pressure increases. The writer has suggested that such an increase in pulse pressure may be a sign of prognostic significance in hemorrhage. In animals, indeed, it is possible to determine accurately by consecutive blood-pressure readings, at what point hemorrhages cease. In practice, however, it is not always so easy to determine systolic and diastolic pressures because of muscular tremors and excessive muscular respiratory movements. Henderson and Haggard have recently suggested that a measurement of the minute volume breathed may be of some prognostic value; as long as the minute volume continues to increase, anoxemia progresses. Obviously, this can only apply in the early stages of hemorrhage.

If, instead of ceasing, the hemorrhage continues to a fatal termination, certain symptoms generally precede death. The skin becomes yellow and dry, the eyes lustreless and the patient sinks into a semicomatose condition. The secretion of urine stops and the rectal temperature falls. The pulse becomes extremely weak and the respiration slow and interspersed with irregular gasps. Convulsive movements may supervene. The heart then becomes very slow and the pulse beats become larger. This is soon followed by cardiac standstill.

When the functions of important organs are seriously interfered with, special features often obscure these general symptoms by their prominence. Thus, in cerebral hemorrhages, the entrance of blood into the cranial cavities causes an increase in intracranial pressure with its attendant symptoms of slow heart, high pressure and Cheyne-Stokes breathing, associated, if the motor areas are involved, with hemiplegia.

In hemorrhage from the lungs, the coughing of blood and respiratory difficulty, the flooding of the lungs with blood and the fear and terror inspired often cause an extreme acceleration of the heart and a rise of arterial pressure.

In wounds of the heart the accumulation of blood in the pericardium leads rapidly to an embarrassment of the cardiac filling similar to that found in cases of pericardial effusions. As soon as the extracardial pressure is great enough to impede the inflow of venous blood, the neck veins fill, the pulse becomes small and varies in amplitude during inspiration and expiration (pulsus paradoxus). Syncope rapidly follows.

SECONDARY SHOCK.

Definition and Classification (Cowell, Dale).—Shock is a condition following surgical operations, trauma, wounds, intoxications or infec-

tions, in which a progressive failure of the body functions, leading more or less rapidly to death, occurs. It is characterized by the symptom-complex characteristic of circulatory failure due to oligemia (*cf.* page 583). Indeed, it is upon the basis of these symptoms, when accounted for neither by the effects of hemorrhage or late infections, that the diagnosis is made. When the symptoms occur shortly after trauma and wounds or during the course of an operation, it is designated as *primary shock*. When, on the other hand, the symptoms are delayed until several hours after an injury or operation, we speak of *secondary shock*. According to Cowell, there is an inherent difference between primary and secondary shock following war wounds. The primary type is either relatively transient and resembles the nervous phenomena of fainting, or is associated with so extensive destruction of tissue as to make continuance of life impossible. In other words, such cases either recover without treatment or are hopeless and, consequently, do not constitute a clinical problem. No doubt, fulminating cases of shock, resulting in speedy death in civilian medical or surgical practice, also represent a variety of acute reflex effects which, through acute cardiac failure, rupture of bloodvessels, emboli, etc., result in prompt death.

When we speak of shock, therefore, in an unqualified way, it is the secondary form which is meant, and to this type laboratory and field investigators have, during the last five years, directed their researches.

According to the causative agent, *surgical, traumatic, wound* and *toxemic shock* have been recognized. While similar conditions may undoubtedly result from the concussion of bursting shells (Hooker), the term *shell shock* has, as a rule, not been applied to these conditions, but is reserved in the literature for more distinctly nervous disturbances, which more or less permanently disqualify the patient but do not lead to circulatory failure and death.

Physiological Changes in Shock.—Extensive investigations (*cf.* Cannon) have shown that practically all forms of secondary shock are characterized by the following physiological changes, viz.: Low venous pressure, low arterial pressure, small pulse, diminished blood volume, increase in the percentage of red cells and hemoglobin, a leukocytosis, reduced alkali reserve, reduced oxygen consumption and lowered basal metabolism. It is evident that, with the exception of the increase in percentage of hemoglobin and red cells and the greater concentration of blood, the changes correspond to those found after extensive hemorrhage.

Cause of Death.—All experimental and clinical observations point toward the probability that death is the result of functional disturbances in the cells of the central nervous system. Practically, death results from failure of the respiratory center, but, if artificial respiration is maintained, failure of the vasomotor center and heart nevertheless soon follow. The symptoms and data indicate, however, that,

even before this, the cells of the cerebrum have been affected to so great an extent that their resuscitation would be quite impossible.

According to modern physico-chemical conceptions it is probable that such loss of function is due to disturbances in the colloidal structures of cells taking place so acutely that they are not recognizable as histological changes, postmortem. This may account for the paucity of essential pathological findings in patients dying from shock. Some investigators (Dolley, Mott) believe that distinctive changes in the nuclear chromatin, size of cells and the staining of Nissl granules occur in the Purkinje cells of the cerebrum, cerebellum and bulbar nuclei. Other histologists, however (Allen, Kocher), attribute such changes to the histological technic and find all changes described within the range of normal. Conservatism further demands that such changes as have been described in the liver, adrenals, etc., be not too greatly stressed.

With such evidence of an involvement of the central nervous system the pertinent questions may be raised: Are these the primary effects in shock and responsible for the associated circulatory and blood changes, or are the central nervous effects secondary to changes in the blood and failure of the circulation? A collation of the available evidence favors the latter hypothesis and makes necessary a critical survey of the nature and significance of the blood and circulatory changes in shock.

The chief evidence that intense nerve stimulation, fear, excitement, exhaustion, etc., are able to produce primary effects on the cells of the central nervous system are: (1) That changes in the cells occur before the blood-pressure has altered, and (2) that immediate changes in conductivity and temperature of the brain take place (Crile and others.) Furthermore, clinical as well as experimental observations indicate that apathy, reduced sensibility, diminution or absence of reflexes can occur before the blood-pressure has begun to fall seriously.

Even if the interpretation given by Crile, Dolley and others to changes in the nerve cells, conductivity and temperature be accepted—which the author for one is not able to do without significant reservations—it does not follow, *ipso facto*, that they necessarily account for or initiate the other functional disturbances which supervene in shock. No one has ever submitted unqualified proof that fear, exhaustion, etc., in animals lead to conditions in which all the physiological changes characteristic of shock are found. Prolonged nerve stimulation usually does not produce shock in animals (Guthrie, Mann, Wiggers). It is true, as the author has found, that apathy diminished sensibility, loss of reflexes and definite weakness in the leg muscles may follow such stimulation; but it is equally true that these animals recover completely from such effects and never lapse into the progressive stage of circulatory failure so characteristic of

shock. It is possible that such effects are comparable to primary shock or shell shock rather than secondary shock. Furthermore, the general distribution of cellular changes, their lack of relation to nerve paths stimulated, the fact that reflex responses from the cerebral cortex are difficult to obtain and their association with many circulatory and toxic conditions make it more probable that such pathological conditions as exist are *the result rather than the cause* of the circulatory phenomena (Pike, Cannon).

Finally, no clear evidence has yet been adduced that the bulbar centers (especially the vasomotor) fail primarily; on the contrary, all experimental evidence indicates that this is entirely a terminal event. Until this time, the center responds to reflex stimulation in an almost normal fashion (Porter) and maintains the peripheral arterioles in a contracted state (Erlanger, Gesell and Gasser, Guthrie, Mann, Morison and Hooker, Seelig and Joseph, Seelig and Lyon).

The Correlation of Experimental and Clinical Shock.—Experimental shock has been produced, more or less successfully, by a large variety of methods which may be placed in one or the other of the following groups:

Group I.—(*a*) Exposure, pinching, manipulation or cauterization of the intestines; (*b*) crushing of muscles, bones, testes; (*c*) extensive burns; (*d*) submitting animals to concussion effects produced by discharge of guns; (*e*) prolonged etherization.

Group II.—(*f*) Massage of stomach with thrusts against diaphragm; (*g*) prolonged compression of inferior vena cava; (*h*) prolonged compression of the aorta; (*i*) pericardial infusions; (*j*) excessive artificial respiration.

Group III.—(*m*) Intravenous and intra-arterial injections of fat emulsions; (*n*) prolonged injection of epinephrin; (*o*) injection of muscle and tissue extracts, peptones and histamine.

With such a variety of procedures for inducing laboratory shock, it is not unnatural that laboratory investigators have been criticized, and have criticized each other (*cf.* Cannon, Henderson, Mann) on the grounds that the conditions thus produced may in no way be comparable to those causing shock in man. With the possible exception of the first group of procedures, which are supposed to reproduce, more or less, conditions obtaining in abdominal operations and trauma, it is obvious that shock is never induced by such means as are outlined in the procedures of Groups II and III.

It must be borne in mind, however, that it has been the task of laboratory investigators, not only to study the nature of the disturbances produced in shock following noxious influences similar to those applying to man, but also to test, by modified experiments, the validity of clues as to the nature and cause of shock so obtained. Indeed, an investigator's ingenuity in evolving experiments, which differ in the method from those which Nature chooses to use, is often

a test of research eminence, provided, of course, that the end-effects are similar to those which occur in pathological conditions in man. Upon such grounds, largely, have such types of experiments as are listed in Groups II and III been studied and, for such reasons, their validity established. While most laboratory investigators, in common with surgeons, have had very hazy conceptions as to what constitutes shock, and, while many have, no doubt, erred in inferring that any condition of low blood-pressure may be looked upon as evidence of shock, the fact remains that after the employment of a large number of these procedures (*not all!*) there results in the end a condition in which *not one but all* the physiological alterations characteristic of shock are present. When this is the case we may fairly infer that conditions comparable to those found in secondary shock in man have been reduplicated. Indeed, it may be argued that such results not only invalidate the arguments as to the dissimilarity of the essential shock conditions, but also really prove that the condition of shock may be induced by a much wider range of noxious influences than ever apply to man in the accidents of every-day life.

For these reasons, the cautious application of the facts obtained from a study of experimental shock, and their correlation with the scientific study of the phenomena of shock in man, has done much to clarify the nature and sequence of the circulatory disturbance and has given us at least a clue to the causative factors.

Changes in the Circulation in Secondary Experimental Shock.—(Produced by Trauma, Intestinal Exposure and Mild Handling—*cf.* Wiggers.) The progress of the circulatory failure, as expressed by the changes in mean arterial pressure and effective venous pressure, by the changes in heart rate and respiration, are shown in a typical experiment plotted in Fig. 194. The changes are in accord with those generally recognized as characteristic of circulatory failure in shock.

Effect of Operative Procedures.—The effects of operative procedures are physiological in nature and probably no greater than those which occur in many reflex effects on the circulation in every-day life. Under light anesthesia the first incision through the skin and fascia of the abdominal wall may produce a temporary cessation or diminution of the respirations, associated with a temporary fall of arterial pressure. The effective venous pressure is unaffected. From this reduced state of arterial pressure, recovery is complete. Upon then extending the incision through the abdominal muscles and peritoneum, the arterial pressure again falls in a similar manner but does not recover completely. The effective venous pressure is often lowered slightly (Fig. 194, *A*).

An analysis of the chart (Fig. 194) corroborated by the more exact optical tracings of the carotid pressure (Fig. 195) shows that the

predominant cause of the blood-pressure decline[1] is a moderate reflex cardiac inhibition which is temporary after the skin incision, but often becomes permanent after the peritoneal incision. The slight

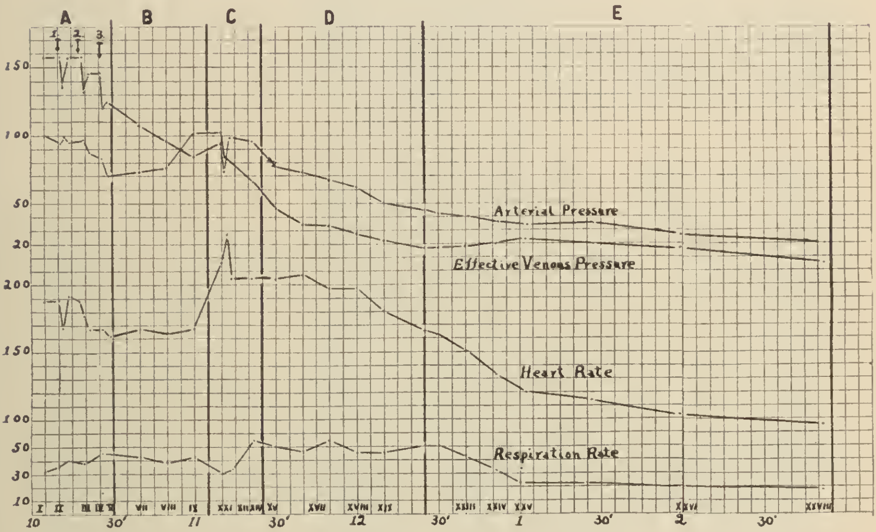

FIG. 194.—Chart showing plotted data of circulatory stages in a case of abdominal shock: *A*, operative stage; *B*, initial stage; *C*, effect of handling intestine; *D*, progressive stage; *E*, complete circulatory failure; 1, effect of skin incision; 2, effect of muscular incision; 3, effect of cutting peritoneum. Roman numerals in lower spaces refer approximately to times when optical records shown in Fig. 193 were recorded.

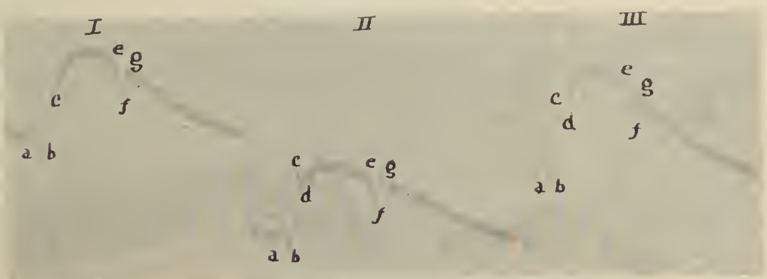

FIG. 195.—(One-half actual size.) Three segments of optical arterial tracings taken before, *I*, during, *II*, and after abdominal incision, *III*. Showing the effect of cardiac inhibition on pressure variations: *a*, *b*, preliminary vibrations; *b*, *c*, *d*, primary vibrations; *d*, *e*, systolic summit; *e*, *f*, incisura; *f*, *g*, after-vibrations.

decrease in venous pressure is no greater than can be directly accounted for by the removal of the intra-abdominal pressure upon the abdominal veins, and it is very doubtful whether the venous pressure is suffi-

[1] *i. e.* during operative procedure.

ciently impaired to affect the systolic discharge. As a rule, this reflex cardiac inhibition leaves the arterial pressure at a level not far from but somewhat below normal.

In the case of trauma, as shown in Fig. 196, every application of violence results in: (1) A fall of mean arterial pressure; (2) a marked acceleration and augmentation of respiration with great expiratory effort; (3) increase in the absolute and effective venous pressures. At first the fall of arterial pressure is accompanied by cardiac accel-

FIG. 196.—Chart showing progressive changes in arterial pressure, effective venous pressure and heart rate following repeated crushing of testes and leading finally to death. Roman numerals refer to optical records of arterial pressure taken at corresponding points. Some of these are shown in Fig. 197.

eration. The optical records at this time show evidence of reduced arterial filling (Fig. 197). The amplitude is greater, the primary wave larger and the systolic portion declines more rapidly (Fig. 197, *II* and *III*). Inasmuch as the effective venous pressure actually increases during the stimulation and the heart accelerates, the diminished filling of the arterial trunks can be attributed only to a reduction in peripheral resistance. After cessation of a single (or sometimes several) attempts at crushing the testes, the respiration becomes slower and shallow, mean arterial pressure returns to a level above

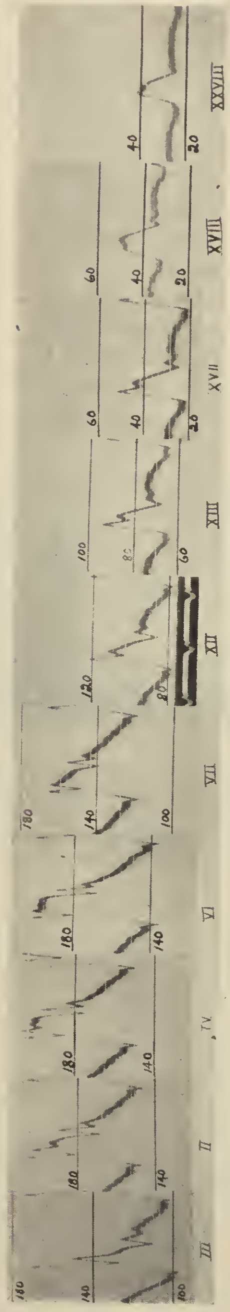

Fig. 197.—Segments of pressure variations in central arteries taken at different stages of fatal circulatory failure by a calibrated optical manometer. Roman numerals correspond to points indicated on chart of Fig. 196.

normal and the optical curves regain their normal contour (Fig. 197, *IV* and *VI*).

These illustrations show how reflex cardiac inhibition and reflex vasodilatation may operate at the time of trauma and during the course of operations, and thus give rise to effects which, if persisting, would give the clinical picture of *primary wound shock*.

Initial Stages of Circulatory Failure.—Upon continued exposure of the intestines to the air, circulatory failure is initiated. As shown in the chart of Fig. 194 *B*, the first gross dynamic change occurs within the first half hour. A careful study of the optical arterial tracings indicates clearly that this must be considered as the initial stage of circulatory failure, even though the effective venous pressure does not alter or even increases and the mean pressure has fallen only to a small extent. These changes are well shown in Fig. 198. A comparison of the last three segments, taken at ten-minute intervals,

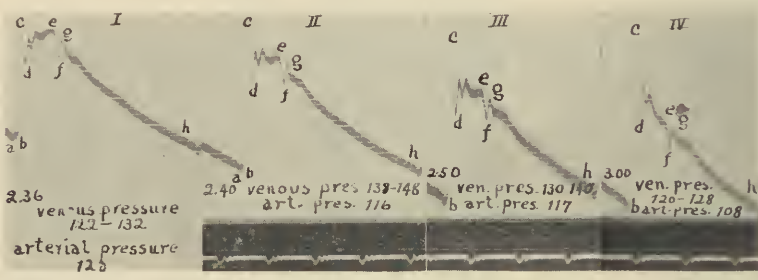

FIG. 198.—(One-third actual size.) Four segments of optical arterial tracings showing essential changes in arterial pressure variations in initial stage of circulatory failure when mean arterial pressure had fallen only slightly. Roman numerals correspond to those of Fig. 194: *I*, normal; *II*, after opening abdomen and intestinal exposure; *III*, ten minutes later; *IV*, twenty minutes later.

with the first segment obtained immediately after exposure of the intestines, shows clearly that a definite reaction has been inaugurated in the vascular system. The preliminary vibration, *a* to *b*, has practically disappeared; the primary oscillation, *b*, *c*, *d*, is much larger and the systolic summit, *d* to *e*, gradually changes from an ascending to a horizontal and then to a descending plateau. The pressure at the beginning of the diastole, *g*, is much lower and, in spite of the lower pressure level, the gradient of the diastolic limb, *g*, *h*, is much steeper. *Such signs are indicative of a diminished distention of the large arterial trunks.* Since these changes occur when the effective venous pressure is still unaffected and intraventricular pressure curves give no evidence of a reduced discharge, they are interpreted as indicative of a reduced total resistance. This need not necessarily be interpreted as due to an arteriole relaxation or to failure of the vasomotor center, but with the evidence of other investigators that the viscosity is not

yet affected, these changes are more probably assigned to capillary dilatation. In favor of such an interpretation are the facts: (1) That similar changes in the optical curves follow the injection of histamine known to produce capillary dilatation (Edwards), and (2) that such a reduction of the total resistance has recently been demonstrated by the Cope method (Forward and Perme).

The Stage of Progressive Circulatory Failure.—The stage of progressive circulatory failure extends from the initial stage to the time that the mean pressure is below 50 mm. of mercury. This figure has been arbitrarily selected by most experimenters as critical because it is then difficult, by known methods, to restore the pressure to normal for any length of time.[1] The duration of this stage is variable, extending from thirty minutes to four hours. The general features are shown in the experiment plotted in Fig. 194, *D*. In this experiment the arterial pressure fell within one and a half hours after intestinal exposure to 50 mm. This was accompanied by a rapidly progressing fall of the effective venous pressure. The heart accelerated. This is typical when vagus tonus is present at the beginning. The respirations increased in rate and amplitude.

The optical arterial pressure curves recorded during this stage become progressively smaller in amplitude and the features characteristic of a great depletion of the arterial trunks become more pronounced. Similar changes occur during trauma, as shown in Fig. 196. Here, also, the corresponding optical tracings (Fig. 197, *VII* to *XIII*) show a progressive decrease in amplitude, indicating that the cardiac discharge was impaired. The heart became progressively slower. At 12.45 P.M. crushing was discontinued and the animal was left unmolested. Both the mean arterial and effective venous pressures continued on their downward course. Ether was discontinued at 1.03 P.M. and the animal never again reacted to painful stimuli until death occurred at 4.17 P.M. The changes in the intraventricular pressure curves are shown in Fig. 192. The initial pressure, *b*, is progressively reduced, the gradient of the pressure curve becomes more gradual and the pressure maximum lower. The volume curves show corresponding changes (Henderson). The rate of diastolic filling is reduced and the systolic discharge is diminished. All of these changes clearly indicate that progressive failure of the circulation, as indicated by the gradual decline of mean arterial pressure, is due solely to a reduced venous return.

The Stage of Complete Circulatory Failure.—When complete circulatory failure becomes established the effective venous pressure is extremely low; the heart begins to slow and thereby further reduces the minute output of the left ventricle. The impression is gained from these experiments that this is the final cause of circulatory failure in shock.

[1] *Cf.* also Cannon and Cattell (Arch. Surg., 1922, **4**, 300).

The progressive changes in the optical arterial tracings during this stage are shown in the last segments of Fig. 197. The pulse form is always of a very simple type and resembles the peripheral pulse in normal animals. The rise is more gradual and the pressure falls markedly during the later systolic period. There is no sharp incisura and the pressure at the beginning of diastole is very low and decreases very little during the diastolic period. Evidently, the peripheral flow ceases entirely during diastole and is limited to the period of systole.

Other Physiological Changes.—During the progressive and final stages of circulatory failure, other functional changes progressively develop. Urinary secretion at first diminishes and later stops entirely. The blood changes are especially interesting. The CO_2 content and CO_2 capacity (alkali reserve) progressively decrease until, during the state of complete circulatory failure, the CO_2 combining power may be reduced by 50 per cent (Gesell, Cannon, Gasser and Erlanger, Raymund, Report of Committee on Surgical Shock and Allied Conditions, England, No. 25; Henderson and collaborators). Whether this is entirely due to a true acidosis from the formation of lactic acid (Macleod) or represents largely a migration of alkali to the tissues (Henderson and Haggard) will be discussed later. The oxygen content remains unaffected in the arterial blood, but is reduced considerably in the venous blood. Oxygen consumption and basal metabolism are reduced (Aub). The effective volume of circulating blood is diminished (Gasser, Erlanger and Meek) and the hemoglobin percentage and red cell counts increase.

The respirations increase in rate and depth and the minute volume respired is considerably increased. Except when trauma or stimuli are actually applied, dyspnea involving forced expiration is, in our experience, rare until the very last stages are reached. Finally, the respirations decrease rather rapidly in amplitude and the animal expires from a final apnea unless artificial respiration is instituted.

Cause of the Reduced Venous Return.—Experiments appear to have established conclusively that the chief cause of the progressive circulatory failure and the attendant nutritional disturbances of all tissues are due to the reduced volume of blood returned to the heart. An explanation of the cause of this reduction, therefore, goes a long way in explaining the causes of shock itself. We may, therefore, examine briefly to what extent the various theories of shock are capable of accounting for these phenomena.

1. *The Exhaustion Theory* (*Kinetic Theory, Crile*).—The validity of the evidence upon which the idea that shock is due to primary exhaustion of the central nervous system has already been examined. According to this theory, a primary progressive exhaustion of the vasomotor center causes a general dilatation of peripheral arterioles, which, it may logically be argued, results in: (*a*) An accumulation

of blood in the veins of the splanchnic area, and (*b*) a fall of arterial pressure. In this manner, the blood trapped in the mesenteric and portal veins fails to return to the heart and, by reducing its filling and discharge, closes the vicious circle by causing a further fall in arterial pressure. The experiments of Erlanger, Gesell and Gasser and Porter indicate, however, that the vasomotor center is not entirely exhausted, and, indeed, not depressed until the very last stages of shock. Furthermore, as previously pointed out, the results derived from a large variety of methods indicate clearly that the peripheral arterioles are not dilated but constricted. Finally, neither in experimental traumatic shock (Erlanger, Gasser, Gesell, Wiggers) nor in wound shock (Wallace, Fraser and Drummond) are the splanchnic vessels found to be congested. It is apparent that the "lost blood" is not accumulated in the veins and that failure of the vasomotor center is at least not usually the primary cause of the reduced venous return.

2. *The Fatty Embolism Theories.* — That fatty embolism of the pulmonary vessels is a frequent cause of death after fractures and after injury to fatty tissue, as well as a sequel of operations, cannot be disputed. Since the symptoms and physiological changes in the circulation after pulmonary embolism are entirely different from those found in secondary shock, however, it is preferable not to include this condition in the category of shock, as has been done by Bissell (*cf.* page 607).

Since the lungs do not act as perfect restrainers of fat entering the venous system, Porter has advanced the conception that shock is due to embolism of the vasomotor center. In favor of this hypothesis is urged the frequent incidence of shock after fractures of leg bones and extensive lacerations of subcutaneous fat. It may be argued, however, that this will not account for cases of shock following laparotomy in lean individuals nor for shock without fractures and without laceration of fatty tissue. Porter has pointed out that fat globules are known to occur in the blood under such conditions, and Mott, indeed, has found fat emboli in the vessels of the medulla itself. Several facts must be taken into consideration in interpreting the significance of such findings. Such medullary emboli are apparently also frequently found in instances (man and animals) where no condition of shock existed (Mott and McKibben); indeed, they seem to be demonstrable whenever a condition of alimentary lipemia exists. It appears that fat in fine emulsion readily separates out under conditions of death or as a result of fixing and staining and is recognizable, postmortem, in all vessels containing lipemic blood.

The chief evidence reported by Porter consists in the fact that not only intravenous but also intra-arterial injections of fat emulsions cause, provided the fat reaches the medulla, a rapid failure of the vasomotor center and a fall in blood-pressure. Other investigators who have succeeded in sending fat to the medulla have not always

been as fortunate in lodging fat so nicely in the vasomotor center. Thus, the fat emulsions injected by the author, when they reach the medulla, seem to have a greater affinity for the respiratory center and cause a rapid death in this way. In the absence of protocols and tracings, there is no evidence that the condition of low blood-pressure produced experimentally by Porter showed also other physiological characteristics of shock. If, however, embolism of the vasomotor center is responsible for the circulatory failure of shock, it is apparent that the reduced venous return must be brought about by the same process of primary vasomotor failure as explained in the theory of vasomotor exhaustion. It, therefore, seems inconsistent of Porter to emphasize on one page of a lecture that the viability of the vasomotor center remains unimpaired to the end, and, on the next page, to postulate that such primary failure resulting from fatty embolism is responsible for the circulatory failure of shock.

3. *The Adrenal Theories of Shock.*—Two conceptions as to the rôle that the adrenal glands and the secretion of its medulla (adrenalin) play in shock have been suggested:

On the basis that the chromaffine tissue, as well as adrenalin content of the adrenals, is decreased in shock (Bainbridge and Parkinson, Corbett, Crile), it has been suggested that the removal of this secretion from the circulation may be the cause of the peripheral dilatation of bloodvessels. The clear-cut observations (1) that the vessels are not dilated, and (2) that the adrenalin secretion remains unaltered during shock (Stewart and Rogoff) more than counterbalance any weight that the suggestion may have.

The idea that shock may be due, on the other hand, to an excessive secretion of epinephrin appeared to be favored by the observations of an increased epinephrin content in the blood in shock (Bedford) and the fact that shock could be produced by prolonged administration of this drug (Bainbridge and Trevan). The latter observation has been disputed by Henderson, who found that death in such cases usually resulted from pulmonary edema or acute cardiac failure. Erlanger and Gasser, who not only corroborated the results of Bainbridge and Trevan but found other typical changes of shock, did not believe that this indicates more than that shock *can* be caused by prolonged asphyxia and anemia of peripheral tissues. Such quantities of epinephrin, as are necessary to produce shock in experimental animals, never exist as a result of stimulated adrenal activity nor are the circulatory changes preceding shock such as result from an increased epinephrin content of the blood.

4. *The Acapnia Theory.*—The acapnia theory (Henderson) states that, as a result of pain or stimulation of afferent sensory fibers, an increase in respiratory volume takes place, thereby decreasing the CO_2 in the alveolar air and blood (acapnia). According to Henderson's earlier conception, this reduces the tone of non-striated muscles and

thereby reduces the extravascular support of the smaller veins and, it may be added, capillaries. This causes, in itself, a stagnation of blood and, through a failure of the "veno pressor" mechanisms, accounts for the reduced return of venous blood. It should be recognized that, thus stated, the acapnia theory was the first to give a logical and possible explanation of the cause of the reduced venous return. In recent years the acapnia theory has been further elaborated (Henderson and Haggard). Evidence has been submitted that the decreased CO_2 content of the blood causes both alkali and fluid to migrate into the tissues, the former causing a reduction of alkali reserve, the latter a concentration of blood or oligemia. Thus, again, acapnia may be supposed to contribute to the reduced venous return in a second way. Finally, the decreased CO_2 tension will tend to depress the respiratory movements and, by minimizing the pressor effect of respiration, may, in a third way, diminish the reduced return. The experimental results obtained from overventilation experiments led Dale and Evans to conclude that the fall of arterial pressure resulting from acapnia is probably due to a relaxation of peripheral arterioles or capillaries. As these effects were elicited while the blood alkalinity increased, they attribute the effects to a primary action of CO_2 as originally accepted by Henderson.

In support of the acapnia theory, Henderson and his associates found that hyperventilation of the lungs and escape of CO_2 from the exposed intestines is primarily accompanied by acapnia and followed by all the circulatory phenomena of shock. The fact that excessive ventilation of the lungs, with the avoidance of acapnia, may produce shock by a mechanical interference with the return of blood to the heart (Janeway and Ewing), no doubt shows, however, that other causes of shock exist. Applying these conceptions to the initiation of shock in man, Henderson pointed out that all painful stimuli or afferent sensory stimuli under light anesthesia cause an increase in pulmonary ventilation and an early decrease in blood, CO_2, and blood alkali. Experimenters are agreed, however, that prolonged stimulation of afferent nerves, even when associated for prolonged intervals with deep breathing, is not a successful means for producing shock (Mann, Guthrie, Wiggers). Furthermore, the decrease in CO_2 content and CO_2 combining power does not appear to occur until circulatory failure has reached a progressive stage (Gasser and Erlanger, Report of the Special Committee on Shock, No. 25, England).

A practical objection to the acapnia theory has been raised by military surgeons, who found that periods of deep breathing did not precede the onset of wound shock. Henderson and his associates, however, draw attention to the fact that a 100 per cent increase in pulmonary ventilation, involving a 50 per cent decrease in alkali reserve, may be scarcely perceptible to the eye (Henderson, Haggard and Coburn, Henderson and Haggard). If this is true, however, the

remarkable fact remains to be explained that, in a variety of diseases, the respiratory rate and amplitude may be visibly increased for days, yet such cases rarely show the symptoms of shock. It would seem, therefore, that this statement should be subjected to further test.

Finally, Henderson and Haggard have sought to show that trauma without excessive pulmonary ventilation does not lead to shock. Thus, gastric massage with diaphragmatic thrusts, which usually produces shock, was found to be ineffective as a shock-producing agency when animals were allowed to breathe an increased percentage of CO_2. It appears, however, that these animals recovered, and in each instance where they failed to induce shock it developed later when CO_2 was withdrawn. It might fairly be asked whether the withdrawl of the CO_2 or the time element played the predominant rôle. In experiments reported to the Committee on Shock, Edwards and the author found no appreciable difference in the ultimate development of shock, whether the animals had a low or high CO_2 content in their blood.

While many of these experiments, therefore, clearly indicate that acapnia is not the sole factor accountable for all cases of experimental shock, it must also be granted that they do not show that acapnia is *in no way* capable of producing all the phenomena of shock. The acapnia theory can, therefore, not as yet be thrown into the discard by those concerned with investigations of shock problems.

5. *The Traumatic Toxemia Theory.*—The traumatic toxemia theory was developed as a result of the practical observation that secondary wound shock is frequently associated with extreme damage or mangling of the muscle tissue, and occurs frequently after operations involving large muscle masses (Quinn, McNee and Wallace, Cowell, *cf.* also Cannon). Furthermore, the impression gained ground that anything that delays absorption from the lacerated area tends to prevent or minimize the incidence of shock (McNee, Sladden and McCartney, Cannon). These observations were followed by laboratory experiments in which it was found that crushing of the limbs of animals, even when the nerves were cut or the spinal cord above the lumbar roots was transected, produced shock and circulatory failure (Bayliss and Cannon, Cannon, Turck). Quite independently a number of French surgeons showed that the injection of muscle extracts also induced shock. All of these observations suggest that the noxious influences causing shock are chemical in nature and carried by the blood. At first it was considered possible that lactic acid formed in muscles and other cells might be the substance primarily responsible, but that theory was soon shown to be erroneous (*cf.* Report of the Special Committee on Shock, No. 25). Then, the significance of certain pharmacological studies of Dale and his associates on histamine began to unfold themselves. They had observed

the paradoxical fact that histamine in large doses causes a profound fall of arterial pressure, due to a reduced peripheral resistance, although in perfused organs it invariably constricted the arterioles. In conjunction with Richards, Dale later showed that this paradox was due to the fact that, while histamine constricts the arterioles by action on its plain muscles, it dilates the peripheral capillaries to so great an extent that their total resistance is actually reduced and the total capillary capacity increased. Upon further investigation, it was shown that this also caused a reduction in the return flow of blood, due, in part at least, to a stasis of blood in the capillaries.

With the demonstration (Abel and Kubota) that histamine or histamine-like substances are formed when tissues are injured or proteins partially digested, that these substances are present in the intestinal mucosa and many glandular secretions, the final link was completed to formulate a toxemic theory of shock which satisfactorily explains not only the onset of various forms of secondary surgical wound, traumatic shock and experimental shock produced by numerous laboratory procedures, but may be extended to include shock following intoxications and infections as well as anaphylactic shock.

Briefly stated, the following sequence of events may be supposed to occur: As a result of tissue injury, manipulation of intestines, intoxication, rapid proteolytic changes in the blood or tissue fluids, or even from prolonged anemia, histamine-like bodies are formed. They at once cause a dilatation of capillaries and reduce their permeability (primarily or secondarily). The immediate tendency of this is to lower mean arterial pressure, but in the initial stages this is compensated by arteriole constriction and in some cases by cardiac acceleration, so that it is evident only as changes in the contour of the central pulse. In the progressive stages, these influences no longer compensate and the mean arterial pressure falls. This further aids the capillary stasis already begun by relaxation of the capillaries themselves and thus reduces the return of venous blood to the heart. To what extent this is aided by an additional passage of fluid from capillaries to the tissues appears to be unsettled. Gasser, Erlanger and Meek observed severe shock in animals in which the blood volumes were reduced only 7 to 17 per cent, although reductions of 40 per cent have been reported in man (Keith). To what factors such an exemia is due is also not entirely clear. The increased intracapillary pressure, no doubt, increases the filtration pressure, and there is evidence that histamine-like peptone may alter the permeability of the capillary wall. But it may fairly be asked, What becomes of such fluid when it leaves the blood stream? Even a 17 per cent reduction in a dog is equivalent to over 150 cc while a 30 per cent reduction in man amounts to nearly 1 liter of fluid. If it is carried away by lymphatic channels, it must eventually be returned to the blood stream. It is apparently not retained in the tissue spaces,

for they do not appear to be edematous. It is, of course, possible that a certain amount enters the serous cavities, but postmortem observations have not generally shown an increase in these effusions. The only reasonable explanation seems to be that through some physico-chemical process they are attracted by the altered colloids of the cells, producing a sort of intracellular edema. If this is true, it is probable that the exemia is not determined primarily or solely by the action of histamine-like substances on the capillaries, but possibly by such factors as: (1) Development of lactic acid in the cells as a result of anemia (Fisher); (2) migration of alkali or salts to the tissues (Henderson); (3) alteration in the metabolism of cells which increases the concentration of intracellular molecules and ions (J. Loeb, Magnus). The attention of pathologists has apparently not been centered, however, on the general cellular changes in shock, for it is probable that the extreme abstraction of water indicated in shock experiments must be recognizable as cloudy swelling or hydrophic changes in the cells. Until the lost water is accounted for more definitely, it cannot be considered as demonstrated that the reduced venous return is partly due to an exemia resulting primarily from the capillary changes induced by histamine-like substances. It must be admitted, however, that the mechanical effects of capillary dilatation and consequent stagnation explains how the reduction in venous return, found early in the progressive stage of circulatory failure, is initiated.

Contributing Factors in Initiation and Development of Circulatory Failure.—While the collated work on shock favors the view that secondary shock is due to the elaboration of histamine-like substances, it is also recognized that this may not be the only process at work. Indeed, it seems probable, both from surgical and laboratory observations, that under certain conditions the injection or absorption of such toxic substances does not produce shock. In the first place, histamine must be injected in relatively large doses in order to produce prompt circulatory failure resembling shock. Small, repeated doses do not result in progressive circulatory failure (Edwards). Consequently, it may be supposed that the rate of absorption after crushing must be sufficiently rapid if shock is to follow. This may explain the absence of shock in many cases of trauma as well as in animal experiments.

In the second place the question may be raised whether the absorption rate from traumatized muscle, for example, is ever so rapid that histamine concentrations in the blood are equivalent to the quantities injected to produce shock. Or, is it necessary that some other factor or factors must coöperate with or precede the absorption of such toxic material? In other words, may we not suppose that the body cells endowed with so many factors of safety have also a certain tolerance for absorbed products? May this tolerance capacity be

reduced or the cells sensitized by other influences before pathological changes take place? While these questions cannot be fully answered, there is a great deal of evidence that various agents act as factors which at least contribute to and possibly even determine whether the absorption of a certain amount of toxic material is sufficient to induce the circulatory changes characteristic of shock.

Ether and Chloroform Anesthesia.—Surgeons and experimenters have definitely obtained the impression that shock develops more rapidly during ether and chloroform anesthesia. Definite evidence has been obtained by Dale that anesthesia sensitizes animals to the action of histamine. Doses ten times as large as those producing fatal shock in anesthetized animals are tolerated by unanesthetized cats. It is possible that this is due to a direct effect upon the endothelial cells (Wallace), but other factors have been suggested as, perhaps, aiding the development of shock. Among these are: (1) That etherization itself often causes a reduction of alkali reserve; (2) that chloroform combines with the red blood corpuscles and reduces the O_2 capacity of blood (Buckmaster); (3) that anesthetics exert a depressing effect on the bulbar centers and thus decrease their resistance to low blood-pressure; (4) that cyanosis accompanying anesthesia reduces the oxygen-carrying power.

Changes in Alkali Reserve.—While the majority of experimental workers are agreed that the reduction of alkali reserve is not a primary cause of shock, it is not so certainly established that it does not favor the initiation or progress of circulatory failure in shock. After a comprehensive investigation the Special Investigating Committee on Shock (England) concluded that "No evidence has been found to support the suggestion that acidosis indirectly favors shock, by facilitating or intensifying the shock-producing agencies, with the possible exception of anesthetics." Among other findings, they recorded that it in no way affected the action of histamine or peptone and the viability of the vasomotor center. A careful perusal of this entire report indicates, however, that this represents a "majority interpretation," in which all experimental evidences not supporting these conclusions are conveniently referred to other causes (*e. g.*, prolonged anesthesia). Consequently, the opinion is on the ascendency that the reduction in alkali reserve, though not dangerous in itself, is an indication of another danger, viz.: An insufficient oxygen supply which must soon lead to tissue death.

It should be borne in mind, however, that, as aside from the not entirely convincing details of the reported experiments, these investigators largely concerned themselves with a decreased alkali reserve resulting from the introduction of non-volatile acids (true acidosis), and did not consider the possible sensitizing effects that a decreased alkali, due to migration of alkali to the tissues as a result of acapnia (Henderson and Haggard), may have on the capillary walls. Nor did

they eliminate the possibilities—well supported in general cellular physiology—that changes in the acid-base equilibrium produced in tissue fluids and cells, or the variable volumes of CO_2 penetrating into cells, may affect the resistance of the cells to a slowed circulation. The possibility has already been mentioned that these processes may determine the retention of water by the cells and so fundamentally be the cause of the exemia. In spite of the general contrary tendency, it does not appear that a reduced alkali reserve, whatever its cause, is without any effect on the onset and progress of the physiological changes which occur in shock; indeed, evidence that administration of alkalies may be beneficial in shock has been presented by Erlanger and Gasser, Cannon, Howell and others.

Direct Loss of Fluid.—Practical observations indicate that the great reduction of blood volumes is not entirely accounted for by capillary dilatation. In many cases it may be attributed to prolonged deprivation of water, sweating, continued oozing or seepage from wounds. The recent experiments of Ringer and Underhill indicate, however, that this does not predispose to shock; on the contrary, in dogs deprived of water histamine-like substances do not produce characteristic concentration effects.

Hemorrhage.—Injuries rarely occur without hemorrhages, either external or into the injured tissues. Too little emphasis has probably been placed on hemorrhage as a contributing factor in shock. The blood lost in operations is often greater than the surgeon supposes (Bazett), while internal hemorrhages often remain unrecognized in accidents. Even small blood losses appear to exert a profound shock-producing effect. Thus, Bayliss found that muscular trauma may not always produce shock in normal animals, but when preceded by a hemorrhage will apparently always do so.

Central Nervous System Disturbances.—While primary disturbances of the central nervous system probably do not directly produce shock, it is probable that certain injuries may hasten the terminal stages. Among these injuries, which at least occasionally add to the gravity of the condition, may be mentioned:

(*a*) Concussion injuries which, by transference of mechanical vibrations, affect the colloidal state of the bulbar cells (Mott) and render them more susceptible to a lowering blood-pressure.

(*b*) Embolism of the vasomotor center.

(*c*) Functional changes in the central nervous system, resulting from reflex, emotional or psychical stimuli.

In short, it is probable that influences which have been suggested as a primary cause of shock in the various theories may, at various times and in different conditions, contribute their share to the development and fatal nature of the total process which we designate as shock.

TRAUMATIC LIPEMIA AND PULMONARY FAT EMBOLISM.

Surgical experience and searching pathological studies have shown that, after fractures, amputation of leg bones and crushing or injuries to subcutaneous fat, globules of unemulsified fat may enter the venous circulation either directly or through the lymphatic channels (Warthin, Bissell). A similar entrance of free fat may also occur in a large variety of other conditions, but, as the amount of fat in the circulation is relatively small, such forms of lipemia are of pathological rather than clinical interest. If the amount of fat thus admitted is large, effective emboli may be formed throughout the pulmonary capillaries. These, by interfering with the transfer of blood from the right to the left heart, give rise to a progressive circulatory failure. Even though the embolism of the pulmonary vessels is not so extensive as to endanger the blood supply of the left heart, some of the fat globules may, nevertheless, work their way through the pulmonary capillaries, enter the systemic circulation and cause emboli in many organs. If, by chance, they lodge in extensive areas of the brain or heart, death from circulatory or respiratory failure may also follow. The possibility that they may lodge in the vasomotor or respiratory center and become a cause of shock has already been discussed.

Pathological Physiology.—When unemulsified or coarsely emulsified oil is injected intravenously into animals, considerable amounts may be tolerated without changes in systemic pressure or circulation. Careful study of optical pressure curves from the right ventricle and pulmonary artery indicate, however, that the pulmonary resistance is increased. The ascending limb of the right ventricular pressure curve increases in height, reaches its summit later and the pressure maximum occurs later during ejection. The pulmonary pressures also rise, particularly the systolic. By virtue of this high pressure in the pulmonary arteries new capillary pathways are probably opened up, however, so that the total volume of blood delivered to the left auricle may not be affected. In consequence, neither the systolic discharge of the left heart nor the systemic pressure are affected (Wiggers).

When fat is injected in larger amounts, however, the picture changes. The arterial pressures fall more or less rapidly, the left auricular pressure falls, pulmonary arterial pressures increase and the right heart dilates and venous pressures increase. Occasionally, relative tricuspid regurgitation supervenes (Warthin, Wiggers). These changes can only mean that the pulmonary vessels are obstructed by fat emboli, a fact verifiable on histological examination. As the pulmonary and venous pressure changes are just the reverse of those found in shock, it is important, for academic as well as therapeutic reasons, to distinguish these types of circulatory failure clinically.

Although pulmonary embolism is apparently primarily respon-

sible for the failure of arterial pressure when fat is injected intravenously, the fact that some of the oil passes through the pulmonary vessels and produces emboli in the systemic circuit (Bissell, Warthin), raises the question whether such systemic emboli may not produce circulatory failure similar to that found in shock. To test this possibility, oils, as such and in emulsions, have been introduced directly into the arterial circulation, thus avoiding pulmonary emboli. The effects of such injections are apparently variable, depending upon where the fat emboli lodge. Two types of experiments may be recognized: (*a*) Those in which a general and extreme fatty embolism of all organs except the brain is produced, and (*b*) those in which embolism of the medullary vessels is produced. In the former classes, incredibly large doses of oil may sometimes be injected without any appreciable alteration in mean arterial pressure. More often, however, the mean pressure rises with each injection and remains high for about an hour. The arterial pressure then gradually declines to and below normal, but, so far as known, the arterial pressure never falls to shock levels, nor is the venous or right auricular pressure reduced. When the emboli pass to the medulla the effects are rapidly fatal. We have already discussed Porter's contention that death is then due to emboli of the vasomotor center. The author's observations indicate that such animals die from a rapid failure of the respiratory center. The arterial pressure after an initial rise falls rapidly and the animal dies within a few minutes. Electrocardiograms show that the heart is not fibrillating and that, therefore, coronary emboli may be excluded as a cause of death. The pressure in the left auricular cavity rises, due to cardiac failure following asphyxia.

Since neither the intravenous nor the intra-arterial injection of fat produces changes in the dynamics of the entire circulation which are comparable to those found in shock following exposure of the intestine, the hypothesis that fatty emboli, either of the pulmonary or systemic vessels, is the cause of circulatory failure in surgical or traumatic shock is not corroborated by experimental work.

Clinical Manifestations.—The symptoms of fatty embolism, of course, depend upon whether the pulmonary circulation is still adequate to feed the left heart and whether, in addition, emboli lodge in vital portions of the heart and brain. Three symptom-complexes may, therefore, appear separately or together (Warthin), viz.: (*a*) Pulmonary, (*b*) cerebral, and (*c*) cardiac.

In all cases, the pulmonary vessels retain the greater bulk of fat entering the veins and, consequently, the pulmonary symptoms depend upon the extent of the embolic process. If large capillary areas are rapidly blocked, death quickly follows, as in acute animal experiments. Extreme cyanosis, a dilated right heart, low arterial pressure and a brief period of dyspnea precede death.

When emboli plug the capillaries more gradually the patient may

live for several weeks. The respiration is augmented and fat globules may be recognized in the sputum (an early positive sign according to Warthin). As embolism and pulmonary congestion progressively increase, moist rales make their appearance and, with the onset of pulmonary edema and hemorrhage, large foamy or bloody masses are expectorated. In such instances the right heart dilates, cyanosis and dyspnea appear. The heart accelerates and systemic pressures fall. The temperature at first falls and may remain subnormal to the end; more usually, however, it increases to 104° or 105° before death.

The cerebral symptoms, which may occur independent of or coincident with the pulmonary manifestations, are: Headache, vomiting, restlessness and hallucinations or apathy and stupor, Cheyne-Stokes respiration, diminished reflexes and pain appreciation, occasionally paralysis, coma and convulsions. Free fat appears in the urine whenever considerable amounts of fat enter the arterial circulation.

The cardiac symptoms may be due to impaired ejection consequent upon the formation of large fibrous clots, or they may occur even more acutely as a result of coronary embolism. In the former instance, progressive cardiac failure, dilatation of the right heart and further increase in venous pressures result. In the latter, ventricular fibrillation may promptly lead to circulatory and respiratory failure.

Clinical and experimental evidence combine in showing that whether death results from pulmonary obstruction or from emboli of cerebral or coronary vessels, the low arterial pressure is always associated with a dilated right heart and great venous congestion—the latter serving as a means of differential diagnosis between circulatory failure due to fatty embolism and that due to shock.

ACUTE MYOCARDIAL INSUFFICIENCY.

Acute cardiac insufficiency, as generally considered in text-books of medicine, is stated to follow a variety of causes, among which are listed: (*a*) Wounds of the heart; (*b*) spontaneous rupture of valves; (*c*) rapid pericardial effusion; (*d*) access of air to heart chambers; (*e*) rapid thrombi formation; (*f*) sudden interference with coronary circulation; (*g*) mechanical interference (?) with heart as a result of pressure on trachea or larynx; (*h*) acute infections; (*i*) certain poisons; (*j*) vagus stimulation in medulla or its terminals; (*k*) overexertion (Osler and McCrae). It is obvious that this comprises a variety of conditions in which death results either as a result of abnormalities of rhythm and conduction or in which mechanical changes in the distribution of blood occur. For that reason it is preferable to designate the cardiac insufficiency that results when the inherent contractile power of the ventricles is depressed by vascular, febrile or toxic influences by the term *myocardial insufficiency.*

Pathological Physiology.—An acute depression of the musculature of the ventricles may be experimentally produced by the action of depressing drugs, such as ether, chloroform, chloral, etc. Is is also a frequent event which terminates many laboratory experiments. Consequently, we may venture an interpretation of the cardiodynamics of acute myocardial insufficiency on the basis of such experiments.

When the heart is thus depressed the ventricles do not discharge their blood completely. Consequently, when this systolic remainder is added to the normal inflow, dilatation of the heart occurs (Socin). Both pulmonary and systemic pressures, therefore, fall and blood accumulates in the right auricle and large veins merging into it. Pressure curves taken from the right and left ventricles rise less steeply and attain a lower pressure maximum in spite of a higher initial endocardiac tension and a greater diastolic distention (*cf.* also page 561, The Hypodynamic Heart). Since both ventricles are affected, it is obvious that pulmonary congestion does not take place, for the systolic discharge of the right ventricle is reduced to an equal degree with that of the left. Stagnation of blood occurs entirely in the venous reservoirs and the liver and the portal pressure are greatly increased (unpublished experiments, Wiggers).

Clinical Manifestations.—It is probable that the effects of primary myocardial failure have not always been clearly distinguished from those produced by other forms of acute cardiac insufficiency listed above. Certain described signs and symptoms, however, so clearly conform to the pathological physiology that they may be considered as quite diagnostic of circulatory failure, due to myocardial failure. The blood-pressure is less and the pulse is small in amplitude. The pulse may be regular or irregular in its rhythm, the latter being incidental. The veins are distended, the liver enlarged and cyanosis may be present. The association of these signs with reduced pressure in the pulmonary circuit and dilatation of *both the right and left heart* serve to differentiate such a form of circulatory failure from pulmonary embolism. The apex-beat is feeble, both heart sounds are feeble over all auscultation areas and may be accompanied by soft murmurs. The pulmonary second sound is feeble or inaudible, in contrast to pulmonary embolism, in which it is accentuated.

TABULAR SUMMARY OF DYNAMIC CHANGES IN DIFFERENT TYPES OF CIRCULATORY FAILURE.

Cause of circulatory failure.	Arterial pressures.	Pulmonary arterial pressures.	Venous pressures.	Right ventricle.	Left ventricle.	First apex sound.	Second pulmonary sounds.
Shock	−	−	−	Smaller	Smaller	−	−
Hemorrhage	−	−	−	Smaller	Smaller	−	−
Pulmonary fat embolism	−	+	+	Dilated	Smaller	−	+
Acute myocardial failure	−	−	+	Dilated	Dilated	−	−

Coincident with these symptoms, others occur which are quite secondary. There is often a heavy feeling assigned to the chest and a feeling of impending dissolution. Vomiting, sudden fainting, sweating, hyperpnea or dyspnea, scanty urine, sleeplessness, delirium, stupor, etc., are among those mentioned.

PLETHORA.

An increase in the total volume of circulating blood (plethora) may result either from an increase in the water constituents alone so that the volume per cent of proteins and cellular elements is decreased (hydremic plethora) or from a proportionate increase in all the blood constituents (true plethora).

Pathological Physiology.—The effects of introducing large quantities of saline intravenously have been carefully studied in laboratory experiments. Such experiments indicate that such injections cause a very slight elevation of mean arterial pressure. Thus, Cohnheim and Lichtheim introduced a quantity of saline equal to 44 per cent of the animal's weight, and Dastre and Loyè increased the blood volume fourfold without any appreciable effect on arterial pressure. Similar observations have been repeatedly made.

Johansson and Tigerstedt and, more recently, C. Tigerstedt showed that the systolic discharge and minute output were increased after venous infusion. Wiggers and Katz have recently shown that such an increase is still possible when the effective venous pressure is raised far above normal, so that the results cannot be accounted for upon the assumption that the experiments were carried out under conditions in which abnormal venous pressures existed. The detailed physiological mechanisms by means of which this is accomplished have already been analyzed in detail (*cf.* page 106).

It might be asked why this greater output does not increase the arterial pressure. In the first place, the statement that arterial pressure is unaffected is not strictly accurate. The systolic pressure is raised appreciably, but the diastolic pressure remains unchanged or falls somewhat, thereby greatly increasing the pulse pressure. The detailed changes in aortic pressure are well illustrated in the pressure curves shown in Fig. 32. The diastolic pressure is not elevated even when very considerable amounts of blood are thrown into the aorta as the result of great and rapid infusion of saline; in fact, during the higher grades of infusion there is a slight tendency for diastolic pressures to decrease. The systolic pressure, as gauged by the summits, *a–b*, increase progressively, however, and this is the more significant since the duration of systolic ejection is prolonged.

The rise of systolic pressure is clearly the effect of the greater systolic discharge. The fact that the diastolic pressure remains unaltered or drops can be accounted for only by a reduced peripheral

resistance in which two factors, a reflex vasodilatation (Sewall and Steiner) and a reduced viscosity of the blood, play a part. By these compensatory mechanisms the arterial pressure is prevented from mounting to an appreciable degree.

If the infusion of saline is slow, the increased cardiac output effectively removes the surplus fluid from the veins and the venous pressure rises only slightly; but if the saline is introduced at a rapid rate, the venous pressure rises and the blood accumulates in the liver (Stolnikow).

When the infusion is stopped, the excess of fluid is rapidly excreted by the glands of the digestive tract and by the kidney, so that the volume of circulating blood soon returns to normal. So, also, it has generally been thought that an osmotic hydremia induced, *e. g.*, by intravenous injection of sugar was only temporary, for, as water passed from the tissues to the blood, it was accompanied by an immediate increase in urinary secretion (Brasol, Starling). A restudy of the question on unanesthetized dogs and for shorter periods of time by Fisher and Wishart demonstrated that, during the second hour after the alimentary ingestion of sugar, the hemoglobin fell 10 to 20 per cent, indicating a plethora, but this was accompanied by an actual diminution in urinary secretion. This observation goes far to show that a condition of plethora, due to osmotic influences alone, may be maintained even under physiological conditions.

All of the above-mentioned experiments are concerned with the establishment of a hydremic plethora. According to Plesch, however, a true plethora may be induced in animals during experimental uranium nephritis. Here the blood volume may equal 16 per cent of the body weight instead of 5.4 per cent as normally. This condition is invariably accompanied by a proportionate increase in red cells and hemoglobin as well as by marked cardiac hypertrophy.

The dynamic effect of a true plethora on the blood-pressure and heart may be studied in an experiment by introducing blood from the artery of one animal into the vein of a second. When this is done the effect upon the cardiac output and intraventricular tension resembles very much that of saline infusion, but both the systolic and diastolic pressures increase, owing probably to the fact that the viscosity of the blood is not reduced as it is in the case of saline infusion. It is evident that the condition of true plethora, on account of the rise of diastolic pressure, increases the load against which the heart has to work more than does hydremic plethora, and, hence, may be expected to lead to cardiac hypertrophy and dilatation sooner than the latter condition.

When this occurs in acute experiments, the ventricles no longer pump out the volumes supplied and, consequently, the left ventricle first becomes dilated both during systole and diastole and later decompensation with pulmonary congestion and right-sided dilatation supervening (C. Tigerstedt).

Clinical Types of Plethora.—While most pathologists and clinicians are apparently agreed that a true plethora exists in conditions associated with increased numbers of red blood corpuscles, opinions have apparently been more divided as to the existence of a hydremic plethora. This doubt has arisen largely as a result of experimental infusion of saline, after which the excess fluid is so promptly eliminated by the various glands of the body that normal blood volumes are quickly restored. Theoretically, it is easy to postulate pathological possibilities leading to increased plasma volume, *e. g.:* (1) When an excessive osmosis of fluid from the tissues without a corresponding increase in urinary secretion occurs; (2) when a deficient urinary secretion, due to kidney disease, exists; (3) when an excessive absorption of fluid from the alimentary tract occurs.

An excessive osmotic attraction for water may possibly explain the greater volume of blood supposed to be found in heavy and continuous eaters. It is possible, indeed, that in these cases, as indicated by the experiments of Fisher and Wishart, the blood is continually surcharged with products of digestion exerting a high osmotic tension without inducing a corresponding urinary secretion. It has been questioned whether the lower capillary pressure in cases of cardiac decompensation may not favor a passage of fluid to the blood stream and so cause a condition of plethora. The fact that the specific gravity of the blood is reduced favors the view that such a hydremic plethora exists, but Starling and Fawcett, who showed that the hemoglobin and red cells are actually reduced, believe that this alone may account for the lower specific gravity without the assumption of plethora.

In nephritis, when albumin is eliminated and the excretion of water is interfered with, Plesch found that the blood volume equaled 10.8 per cent of the body weight as compared with the normal average of 5.3 per cent when edema was not present.

The third cause of plethora, *i. e.*, increased absorption of fluid from the alimentary tract, an absorption in excess of the excretion may be responsible for the plethora supposed to be present in excessive beer drinkers.

Clinical Manifestations.—The clinical manifestations of hydremic plethora are not always definite and the diagnosis cannot be made from appearance alone, the so-called "plethoric habit" being no criterion of the circulation volume. It is generally assumed, however, that hydremic plethora exists when corpulence, ruddy complexion, full and dilated superficial vessels are associated with an enlarged heart, a pulse of larger amplitude and some elevation of systolic pressure. The reliability of this assumption is undoubtedly increased when the history of the patient indicates an excessive consumption of fluid or when evidences of nephritis exist.

The diagnosis can be definitely settled only when the actual relation of blood volume of body weight is determined.

Until recently, no reliable methods for determining the blood and plasma volumes have existed. Of the methods now in use, which may, with some degree of exactness, be employed for such purposes, those which are based upon the following principles are most commonly employed: (1) Those based upon the determination of the dilution of known amounts of substances soluble in the plasma after injection, *e. g.*, vital red (Keith, Rowntree and Geraghty) or acacia (Meek and Gasser); (2) those based upon the dilution of known amounts of carbon monoxide when inhaled (Plesch, Haldane).

It is generally stated, after Welcher, that the normal blood volume is equal to 1/13 (7.6 per cent) of the body weight. More recent investigations by the methods above indicated are not all in agreement with this figure, however. Thus, determinations made by the CO method (Haldane, Plesch) indicate that the blood volume on an average equals about 1/19 (5.3 per cent) of the body weight. The studies of Keith, Rowntree and Geraghty, and also those of Bock, on the other hand, indicate that Welcher's figures are correct. They found the average blood volume to be about 5350 cc, or 85 cc per kilo, which, if calculated upon the basis of relation to body weight, equals about 1/11.4 (8.8 per cent). The plasma volume they find to be about 5 per cent, or 1/19.6 of the body weight. Salvesen, using a procedure described previously by Van Slyke and himself, found extreme ranges to run from 1/14 to 1/17 of the body weight. Investigation showed small differences between children and adults. Also, there is little sexual variation. An interesting observation, reported by Keith, Rowntree and Geraghty, is the definite increase in both blood and plasma volume during pregnancy.

The application of these methods to pathological conditions in which increased blood volumes may logically be expected, have yielded results which may briefly be reported: After hemorrhage the increase is not great and is sometimes not present at all. It also varies with the interval elapsing after the hemorrhage before the results are obtained. In primary anemias (pernicious anemia, chlorosis), where it may be anticipated that the decrease in red cells is compensated for by an increase in plasma volume, results have been somewhat contradictory. Using the carbon monoxide method, Smith and also Boycott found figures which indicate that the blood volumes are increased in both of these conditions. As Boycott points out, however, such differences obtained by the carbon monoxide method may be more apparent than real, and the probabilities are that the values so found are somewhat exaggerated. This is also the conclusion reached by Bock, who found plasma volumes equal to 5.4 per cent, or 1/18.5, of the body weight in cases of pernicious anemia having hemoglobin volume from 43 to 59 per cent. In comparing the blood and plasma volumes in these cases, they always found the latter normal, which leads to the conclusion that the plasma volume is

not increased during these forms of anemia, and that, therefore, a condition of hydremic plethora cannot be said to exist. It has frequently been noted that whenever the number of red cells increase at high altitudes an increase in blood volume occurs. In 3 cases of pathological polycythemia, Bock found a total volume equal to 1/7.3 of body weight. On analysis it was found, however, that the plasma fraction equaled 1/16.2 to 1/21.2 per cent. They conclude, therefore, that the increased volume in certain cases is almost entirely due to the increased number of cellular constituents.

In diabetes mellitus, a condition in which a hydremic plethora may be postulated, owing to the increased amount of dextrose in the blood, normal plasma volumes were found by Bock. In cardiac and nephritic disorders accompanied by edema it is not impossible, as Krehl points out, that there is also an edema of the blood. Plesch and Boycott apparently confirm this conclusion in their experimental work on uranium poisoning accompanied by edema. Plesch, furthermore, reports cases of nephritis in edema in which the blood volumes varied from 7.87 to 10.8 per cent of body weight. Keith, Rowntree and Geraghty failed, however, to find an increased blood or plasma volume in cases of hypertension and nephritis; indeed, the blood volumes were often rather low. In cases examined by Bock, the blood-plasma volume remained normal as related to body weight. While it is yet too early to draw final conclusions as to the frequency with which increased volumes of blood and plasma are primarily responsible for changes in the dynamics of the circulation, such as are produced experimentally, the observations so far reported make it perfectly clear that while there is a tendency for acute variations in plasma volume to take place, the compensatory mechanisms are usually sufficient so that they do not often become a feature of chronic disease.

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CHAPTER XXVII.

MECHANICAL IMPAIRMENT OF CARDIAC ACTION.

INFLUENCES AFFECTING THE POSITION OF THE HEART.

The heart is suspended in the thorax by its large vessels and its long axis is prevented from assuming a vertical direction only by the fact that it rests upon the diaphragm below and is supported by the lungs laterally. It is inclosed within the pericardium, a relatively inelastic structure which is attached to the large vessels at the base, continued upward with the cervical fascia and merged with the central tendon of the diaphragm below. It is further anchored to the sternum and vertebral column by bands of connective tissue which are often sufficiently well defined to merit the term "ligaments." Owing to the intimate relation existing between the heart and the diaphragm, the position of the former is determined by the movements and height of the latter. A change occurs even during respiration. The inspiratory descent of the diaphragm causes the axis to become more vertical, as electrocardiographic and roentgen-ray studies show. The apex and base both move down, the heart shadow elongates, while the right and left borders move toward the right (Fig. 13).

Pathological Changes in the Position of the Heart.—Aside from congenital variations and the pressure of intrathoracic tumors, the position of the heart may be altered either as a result of an abnormal position of the diaphragm or of traction by pathological adhesions.

When the position of the diaphragm is very low, as frequently occurs in emphysema (Fig. 199), in enteroptosis with loose abdominal walls, etc., the heart occupies a median position, while its contour is long and narrow. Because the larger vessels are stretched, the actual boundaries of the heart may be displaced below the fourth intercostal space.

When the entire diaphragm is pushed upward, as in cases of ascites, pregnancy, meteorism, etc., the heart assumes a more horizontal position. This is essentially an exaggeration of what normally occurs during expiration. If only the left dome of the diaphragm is pushed upward (as in cases of gastric inflation, tumors of the fundus, etc.), the apex is raised, and when the left dome rises higher than the right, the heart is pushed toward the right. Ascent of the left dome, due to a retraction of the left lung, such as takes place in incipient tuberculosis, often causes the two domes to be equal in height and results

in a median placement of the heart. The elevation of the right dome, *e. g.*, by an enlarged liver, pushes the heart horizontally to the left side.

The position of the heart may be influenced by intrathoracic processes which exert a traction or pressure in a certain direction. Thus, any extensive atelectasis, pneumothorax, bronchostenosis, etc., of one side causes a movement of the heart toward that side. On the other hand, pleural effusions, aneurysms, etc., cause by pressure a displacement of the heart in the opposite direction. Adhesions between pleura and pericardium also tend to draw the heart to the side upon which they occur. Furthermore, adhesions between the lungs and diaphragm may secondarily affect the position and respiratory movements of the heart. The writer has demonstrated in dogs that the

Fig. 199.—Roentgenogram showing the effect of a low diaphragm on the position of the heart. (After Grödel.)

posterior portion of the heart and venæ cavæ descend more than the anterior aspects of the base during inspiration, while the anterior aspect of the apex moves forward and, consequently, slightly upward. The descent of the base is largely due to a traction on the ligamentum pulmonale (a double fold of the pleura continuous with the pleura pulmonalis, and passing downward from the roots of the lung to its vertebral and diaphragmatic attachments), which causes the roots of the lung, the pulmonary vessels and, through them, the base of the heart to move downward. In man, the ligamentum pulmonale is not continuous with the diaphragmatic pleura, but adhesions between the pleura and diaphragm are frequently seen in the dissecting-room, which must act in a similar manner in drawing down the large pulmonary vessels and base of the heart.

Clinical Manifestations.—A low position of the diaphragm and a vertical position of the heart are attended by clinical symptoms which indicate that the output of the heart is deficient. The patients suffer from dizziness and tire easily. The extremities are cold and the pulse is small, rapid and weak. These symptoms may be associated with a lax abdominal wall and definite evidence of enteroptosis, or they may be found associated with long thoraces, and emphysematous changes in which the diaphragmatic excursion is markedly diminished. In some cases, careful observation shows that the abdominal wall is actually drawn in during inspiration (Wenckebach). In these cases, the heart is often hanging, as it were, by the large vessels and constitutes the so-called "hanging heart." Owing to the traction that each systole then has on the trachea the patient may experience a distinct systolic tracheal tug resembling that obtained in aneurysm, or, since in some cases the condition is more pronounced during inspiration the tug may be felt only during that phase. There may also be an inspiratory filling of the neck veins, as in adhesive pericarditis, or the arterial pulse may be small during inspiration, due to a traction on the aorta.

A high position of the diaphragm causes the heart to lie more horizontally, hence the heart dulness is often increased and the apex displaced to the left. The pulse is also small and poorly filled, but there are no signs of edema, venous engorgement, etc. The condition is sometimes associated with tachycardia, and premature systoles are often associated with it. Changes in the function of the heart can generally be determined by establishing the electrical axis during the R deflection (*cf.* pages 281 and 287).

CONDITIONS AFFECTING THE PULMONARY CIRCULATION.

The resistance offered to the blood flow in the pulmonary circuit affects not only the work of the right ventricle, but may also determine the output of the left heart and to a certain degree the arterial pressure. It has been generally supposed (Tigerstedt) that a large share of the pulmonary circuit can be occluded without affecting the pulmonary arterial or the left auricular pressure. This has been accounted for as due to a compensatory opening up of the more peripheral pulmonary vessels which are normally collapsed to a certain extent. The writer has demonstrated, however, by more delicate manometers, that the clamping of a single branch of the pulmonary artery in animals causes an increase in the maximal pressure both within the right ventricle and in the pulmonary artery. The initial tension and steepness of the intraventricular pressure rise remain unchanged, but the ejection period begins and ends progressively later and the summit is reached more slowly. These experiments indicate that wherever an increased resistance occurs,

such as must follow pulmonary embolus, sclerosis and probably infiltration in pneumonia, the right heart having a greater afterload to overcome, must respond with a more vigorous contraction. If this persists, it can be readily appreciated how the right-sided hypertrophy so generally associated with this condition arises. (For details *cf.* page 569.)

A similar increase in vascular resistance probably occurs in pneumonia, chronic tuberculosis, atelectasis and compression from pleural exudates, accounting in part for the hypertrophy of the right ventricle (Hirsch).

It is not necessary to assume that the filling and output of the left heart are interfered with in all conditions in which the resistance is increased and the right heart action augmented. Thus, it is found that ligation of a section of pulmonary artery causes, synchronous with the elevation of pulmonary arterial pressure, no diminution in the left auricular pressure. This is so, partly because the velocity of flow is increased through the channels still open. This is in accordance with clinical findings, namely, that the blood-pressure is not low and the flow through the heart is not diminished or may be even increased (Stewart) in cases of advanced tuberculosis and in pulmonary emphysema.

Acute Pulmonary Edema.—In contrast to edema developing in other portions of the body, pulmonary edema is characterized by its acute onset, its rapid development, occasionally its equally quick disappearance and its occurrence as occasional complications of a large variety of acute and chronic diseases. Thus, it is found as a complication of acute infections (pneumonia, influenza, typhoid fever, etc.), chronic myocardial and valvular diseases of the heart, arteriosclerosis and renal disease, and is a direct consequence of the inhalation of a variety of so-called "war gases," *e. g.*, phosgene, chlorine, chlorpicrin, etc.

In research, it is frequently observed as a complication of prolonged experiments, but it has also been produced in a variety of ways, *e. g.*, by: (*a*) Intravenous emboli finding lodgment in the pulmonary circuit (Kotowschtschikow); (*b*) intravenous injection of toxic chemicals and drugs (*e. g.*, acetic ether, silver nitrate, iodine preparations, epinephrin, muscarin, etc.) (Grossmann, Löwit, Meltzer, Emerson, Miller and Mathews); (*c*) injury to the ventricular myocardium (Welch); (*d*) injection of large quantities of saline (Cohnheim and Lichtheim); (*e*) inhalation of irrespirable gases and vapors (*e. g.*, ammonia, chlorine, hydrogen sulphide, bromine, phosgene, etc.) (Lehmann, Pettenkofer, Miller and Mathews, Winternitz, Warthin, etc.); (*f*) mechanical obstructions in the left auricle and pulmonary circuit (*e. g.*, intense mitral stenosis, obturation of the left auricular cavity, ligation of pulmonary veins, etc.) (Rosenbach, Lichtheim, Grossmann, Löwit).

As the aim of experimental work has been not only to determine the conditions under which experimental edema may be produced, but also to ascertain whether such causes can possibly operate in man, it is particularly necessary to analyze the net results of this experimental work from the latter angle. It is probable that two types of pulmonary edema must be recognized.

Mechanical Edema Due to Passive Congestion.—When the resistance within the pulmonary veins is experimentally increased, as by pulmonary emboli, ligation of pulmonary veins, obliteration of the left auricular cavity and occasionally as a result of mitral lesion and increased aortic resistance, not only is the pulmonary arterial pressure raised but the intracapillary pressure is also increased. Consequently, a greater filtration pressure, which might be considered a fundamental cause of edema, exists. A careful review of experimental evidence can leave no room for doubt that if the pulmonary capillary pressure is sufficiently increased through these means for sufficiently long intervals of time, a transudation of blood serum into the pulmonary alveoli will occur. On the other hand, there is little reason to believe that, aside from rare instances in which extensive pulmonary emboli or left auricular thrombi occur, mechanical forces can ever operate in the body which are comparable to those produced in experimental animals. In dynamic considerations previously analyzed, it has been pointed out that mitral lesions and increased aortic resistance, for instance, do not produce back-pressure effects which extend to or beyond the capillary system. Indeed, as pointed out on page 171, the heart possesses remarkable ability to prevent the pressure within the pulmonary circuit from rising to any marked degree.[1]

It is, therefore, improbable that a degree of pulmonary congestion sufficient in itself to cause a transudation of the plasma constituents into air cells can be produced in these ways.

There is, however, another mechanism capable of doing this—one that was recognized by Welch even before we understood the regulatory physiological mechanisms by means of which the discharge of the right and left ventricles are kept constant at all times (*cf.* page 171). If, for any reason, the systolic discharge of the left heart is even slightly less than that of the right, *i. e.*, when there is a disproportion between the output of the two ventricles, blood must accumulate in the pulmonary circuit in increasing amounts and lead to a great augmentation of capillary filtration pressure (Welch). Such a result has been demonstrated experimentally to follow mechanical injury of the left ventricle and probably occurs clinically when the contraction of the left ventricle is chiefly affected by toxic and circulatory changes in disease.

Early failure of the left ventricle may occur, moreover, as a purely

[1] For detailed discussion *cf.* Wiggers (Physiol. Rev., 1921, **1**, 256).

functional affair, *e. g.*, when it is required to react to strain beyond its ability or increased volume of inflow for long intervals of time (Starling and associates). Finally, it must be borne in mind that, while increased work of the left heart, or mitral lesions, each by itself, causes no pulmonary engorgement extending to the pulmonary artery, they *are* capable of doing so when such derangements occur simultaneously (Wiggers and Feil). It is probable, therefore, that marked pulmonary congestion may be due to a disproportionate working capacity of the two ventricles, not only when the myocardium of the left side is deleteriously affected, but also when dynamic events combine in such a way that the systolic discharge of the left ventricle no longer equals that of the right.

Toxic Edema Due to Permeability Changes in Pulmonary Capillaries.—Experimentally, the pulmonary capillaries may be damaged so that their permeability changes and they allow plasma to pass even under normal capillary pressures. The injurious substances may be absorbed from the alveoli or transferred by the blood stream. To the first class belong the types of pulmonary edema resulting from inhalation of lethal war gases. The consensus of opinion is to the effect that in this condition damage to the pulmonary epithelium and the capillary walls is a primary effect. Transudation of serum gives rise to pulmonary edema, on the one hand, and to a concentration of the blood, on the other. In the course of so-called inflammatory types of edema, which Sahli insisted is the common type in man, the noxious agents affecting capillary permeability are probably carried through the blood streams. Of toxic substances affecting the capillary walls so as to increase their permeability, various agents have been pointed out. Certain bacterial split-products themselves may have a lymphagogue action, or substances may be formed as a result of metabolism which alter the normal physico-chemical relations of the endothelial cells. Death, under these conditions, may be accounted for in either one of two ways. The edematous condition of the lungs may not permit the interchange of gases in these organs, so that the animal asphyxiates or the individual, so to speak, drowns in his own fluid. The observations of Winternitz and Lambert indicate, however, that this is not the chief factor. On the other hand, the reduced volume of blood affects the systolic discharge of the heart and reduces the minute volume to so great an extent that even if oxygenated there is not a sufficient supply to the tissues, and death eventually results from anoxemia alone.

PERICARDIAL EFFUSIONS.

Pathological Physiology.—A small quantity of fluid is normally present within the pericardial sac, but this is without effect on the circulation. It has been demonstrated repeatedly, however (Cohnheim,

Starling, Lewis, Cannon), that a marked increase in pericardial fluid causes a rise of venous pressure, because fluid is prevented from entering the heart. The systolic discharge of the heart is thereby reduced and the arterial pressures fall. The amount of pericardial fluid necessary to affect the venous pressures and minute output appreciably, as also that required to prevent filling and discharge entirely, depends upon the height of the supplying pressure (Kuno). Thus, in an experiment in which the venous pressure was 90 mm. of blood, Kuno found that 3 to 5 cc caused a recognizable decrease in the discharge of a dog's heart, whereas 15 cc were required to produce a proportional decrease when the venous pressure was 240 mm. of blood. The effects upon the arterial pressure are interesting, as the peripheral resistance was kept constant and blood-pressure effects were solely determined by the minute volume discharged by the left heart. Kuno found that the arterial pressure falls only slightly during these earlier stages, but when a certain amount, roughly estimated to equal 70 per cent of the volume, which causes the heart to entirely cease expelling blood has been introduced an abrupt fall of pressure results.

Experimental work carried out on intact animals by Katz and Gauchat indicate that much larger quantities of fluid may by introduced at venous pressures normal to the animal before the systolic or diastolic pressure falls. This may be interpreted as showing that the heart within the body with anatomical relations left intact has a larger factor of safety, as regards being choked off by increasing pericardial effusions, than the perfused heart. These observations also accord with those published by Starling. This investigator allowed varying quantities of a bland oil to enter the pericardium and observed the simultaneous effects of different quantities on the arterial, venous and portal pressures. These effects are indicated in the following table:

Amount of oil introduced, cc.	Arterial pressure, mm. of mercury.	Portal venous pressure, mm. $MgSO_4$.	Inferior vena cava, mm. $MgSO_4$.
–	90	128	36
20	90	128	36
40	90	128	40
60	Slight fall	128	58
70	90	134	76
90	56	160	124
100	26	180	170
Heart stopped	15	215	215
Removed fluid to 0	146	322	36
Ten minutes later	84	148	36

A perusal of this table indicates that, though the venous pressure is raised, as much as 70 cc can be injected without affecting the arterial pressure. The decreased output is apparently compensated for by a vasoconstriction. The portal pressure also rises, due to a similar vasoconstriction and to the higher venous pressure. When more

than 70 cc are injected, arterial pressure rapidly falls, for the reduction in output is then so great that it cannot be counterbalanced by any further peripheral vasoconstriction. The portal pressure rises steadily with the venous pressure. When the pericardial fluid is removed, the arterial pressure rises suddenly to a much greater height than before and the portal pressure rises still higher, indicating that a great constriction has occurred (Starling, Kerppola and Walle).

While such experiments are capable of analyzing the fundamental dynamic modifications of the circulation, they do not take into account the accessory changes that occur with the phases of respiration. For this reason, Katz and Gauchat have recently investigated the effects of increasing amounts of pericardial fluid in animals breathing naturally with their thorax closed. They found that the slight or barely perceptible variation in pulmonary pressure found normally during inspiration and expiration became more and more accentuated as the pericardial fluid increased, until finally no pulse beats occurred at all during the phase of inspiration. In this way, they reproduced the *paradoxical pulse* so frequently associated with this condition clinically. After a searching investigation they arrived at the following interpretation of this interesting dynamic event:

When the inelastic pericardial sac is filled with fluid under a positive tension, the structures enclosed with it, *i. e.*, the auricles and ventricles, are much less affected by respiratory variations of intrathoracic pressure, that is, they become in effect extrathoracic structures. The entering veins, on the contrary, are still subject to such variations, consequently, when intrathoracic pressure decreases during inspiration, the reduced effective pressure causes blood to accumulate within them and, therefore, the heart is filled imperfectly or not at all during this respiratory phase. The reduced or negligible discharge is the cause of the small or absent pulse found during inspiration.

Clinical Signs.—Patients with pericardial effusions may show few symptoms or they may be afflicted with fainting attacks. Upon examination, the interspaces are often found to bulge if the effusion is great. The impulse is either diffuse or absent. The auscultated sounds are dull, muffled or indistinguishable. Under fluoroscopic examination, all differentiation between auricle, ventricle and aorta are lost and roentgen-ray plates give a characteristic triangular shadow with its base down which corresponds to the dulness made out by percussion. The lung areas are dark, owing to their congestion (Fig. 200). After the removal of the exudate, the heart pulsations appear normal and the shadows regain their clearer outlines. A study of the circulation when effusions are present reveals a high venous pressure and a positive venous pulse—often accompanied by an enlarged liver. The arterial blood-pressure is low and the pulse pressure small. The pulse amplitude decreases during inspiration

(pulsus paradoxus). It disappears entirely after the exudation is removed and reappears when it reaccumulates.

Considerable interest is attached clinically to the precise location of pericardial effusions. Recent investigations (Williamson) indicate that fluid accumulates first along the lower margin of the heart,

Fig. 200.—Roentgenogram from case of pericardial effusion. (After Grödel.)

i. e., on the diaphragmatic surface, and this may be the only place that fluid is found when effusions are not large. This space filled, it extends over the large vessels at the base, and only as this happens may retrosternal dulness be elicited. The anterior surface of the heart may remain entirely uncovered, so that a pericardial friction sound may still occur.

PERICARDIAL ADHESIONS.

In place of a total reabsorption of the exudate and fibrin, it not infrequently happens that the latter undergoes organization and forms strong elastic bands, anchoring the epicardium to the pericardium. These bands may pass: (*a*) Posteriorly to the mediastinal tissue; (*b*) below to the diaphragm; (*c*) anteriorly to the sternum; (*d*) laterally to the pleura.

Clinical Manifestations.—The clinical signs and symptoms are as varied as the nature of the adhesions and, consequently, the diagnosis is most unsatisfactory. Many cases pass undiscovered to the postmortem table. The symptoms and disturbances created depend less upon the number and extent of the adhesions than on their location and anchorage (Riegel). Disturbances arise when the movements and normal contractions of the heart are interfered with or when the entrance or exit of blood is mechanically blocked.

According to Riegel, the adhesions may be divided, clinically, into two groups, namely, those showing general disturbances and those showing definite physical signs. The general disturbances are essentially those of cardiac insufficiency, palpitation, dyspnea, cyanosis and sometimes edema. They offer nothing distinctive upon which to base a diagnosis. The cases in which definite signs are present are also difficult to diagnose, since the signs vary so much in different cases. It is desirable, therefore, to limit ourselves to the typical effects of different adhesions.

The character of the apex-beat is sometimes altered when anterior adhesions occur. It may not be displaced as normally, with a change in body position, or there may be a strong systolic retraction of the interspaces. When the heart is absolutely fixed to the surrounding structures of the posterior mediastinum, the anterior wall and to the diaphragm, there is with each systole a retraction of the lateral and lower interspaces opposite which the diaphragm is inserted (Broadbent's sign). This is of greater significance when the cartilages and lower end of the sternum are drawn in as well during each cardiac systole. In some cases, an inspiratory inward movement of this region occurs (Wenckebach).

Posterior adhesions usually encircle or compress either the vena cava or aorta in inspiration. If the former is the case, then the extrathoracic veins fill in inspiration and the output of the heart decreases so that the arterial pulse becomes small in that phase. An entire wave may be dropped in inspiration when the adhesion causes a traction on the aorta and produces a stenosis or kinking (Kussmaul's pulse).

If the adhesions are firmly attached to the lungs, their deflation may cause a kinking of the artery during expiration and so account for the dropping of an expiratory beat (Riegel's phenomenon).

If the adhesions interfere mainly with efficient contraction of the right side of the heart, venous engorgement is prominent, while, if the left ventricle is affected, dyspnea and pulmonary edema are often brought on.

AUGMENTATION OF INTRATHORACIC PRESSURE.

An augmentation of intrathoracic pressure occurs under all conditions in which the egress of air is interfered with in expiration, either through a contraction of bronchioles, as presumably occurs in asthma, or in some forms of laryngeal stenosis.

Clinical Physiology.—If the intrathoracic pressure of an animal is increased by rendering free expiration more difficult, it results, first, in a rise and later in a fall of the arterial pressure. The rise of arterial pressure can readily be shown to be accompanied by an increased cardiac output, the subsequent fall by a decreased dis-

Fig. 201.—Effect of a deep inspiration, *I*, and a forced expiration, *E*, with mouth and nose closed, on the radial pulse, recorded optically (Valsalva's experiment).

charge of the heart. Since the venous pressure in the extrathoracic veins rises and the effective right auricular pressure falls (personal observation) in the latter case, the fall of arterial pressure is associated with an impeded venous return occasioned by the high intrathoracic pressure.

Clinical Significance.—A similar effect on the circulation results in paroxysms of asthma. The pulse is rapid and dicrotic, the veins congested and arterial blood-pressure low. For purposes of study, a similar reaction can be demonstrated in normal man by carrying out the well-known experiment of Valsalva, which consists in making a forced and prolonged expiratory effort after a preliminary deep inspiration. The radial pulse tracing then shows (Fig. 201, *E*) that the base line at first rises and later, if expiration be maintained, falls somewhat, the pulse wave at the same time becoming hyperdicrotic. The rise has been shown by Lewis to be due to an actual increase in arterial pressure and not, as sometimes supposed, to a congestion of the venæ comites under the button (Hill, Barnard and Sequeira). The fall of the curve associated with hyperdicrotic waves following the rise of pressure is usually explained as indicating a fall of arterial pressure due to the reduced venous return to the heart and a subsequently decreased systolic discharge. This has been questioned by Lewis, who contends that, owing to a simultaneous contraction of abdominal muscles, the filling of the heart in man is never impaired and the arterial pressure remains high. Upon this point, however, his experiments are not convincing. Tracings taken with optical apparatus indicate that the pulse amplitude becomes smaller at the same time that the entire curve falls, and the dicrotic notch becomes larger. It seems more plausible, therefore, to regard the prolonged rise of intrathoracic pressure as interfering with the venous return and so reducing the output and the arterial pressure.

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CHAPTER XXVIII.

AFFECTIONS OF ARTERIES.

ANEURYSMS OF THE THORACIC AORTA AND BRANCHES.

By an arterial aneurysm we understand the cylindrical, saccular or globular enlargement of an artery that follows the diminished resistance of its walls to the internal arterial pressure. Although aneurysms may develop in any artery, we shall confine ourselves to those affecting the intrathoracic aorta, both because this vessel is most frequently attacked and because an aneurysm in this situation produces the most pronounced changes in the circulation.

Pathological Physiology.—An aneurysm never develops without some weakening of the arterial wall. Apparently, the primary cause is found in an inflammation of the vasovasorum, which travels inward toward the media. Because of the deficient blood supply and toxic influences, a degeneration of the elastic tissue and muscle fibers occurs which diminishes the elasticity of the vessels. Hence, with every arterial impact there is less and less return to the normal condition and the artery undergoes a progressive expansion.

The infection most frequently concerned in these changes is syphilis. Occasionally, these changes are secondary to violent strain, which may rupture the intima and thus lead to local weakening. Emboli of the vasovasorum and external injury or erosion of arteries are less common causes.

Of considerable interest is the mechanism of aneurysm formation, as a result of compression. It has been frequently noted, clinically, that when the subclavian artery is compressed by a cervical rib, aneurysm or dilatation of the artery occurs peripheral to the point of compression. Halsted has carried out some interesting experiments which show that a similar dilatation appears when an artery is compressed by a metal ring. He explains their formation as due to two factors, viz.: (1) The action of abnormal whirlpools produced in the dead pockets distal to the constriction, and (2) the lowered pulse pressure to which the vessels are submitted.

The shape of the aneurysm is determined primarily by the area involved, much, as in glass blowing, the protrusion upon blowing becomes globular, cylindrical, symmetrical or asymmetrical, in accordance with the area softened. The shape is sometimes secondarily altered by contact with external structures which distort it, or by irregular and secondary arterial necrosis which often gives a somewhat lobulated character to the sac.

The progressive bulging is counteracted by two forces. The intima, devoid of bloodvessels, undergoes a compensatory thickening, which may be so extensive in small aneurysms as to strengthen the wall adequately and "cure" the condition. In larger aneurysms this process is rarely sufficient. In these cases a deposition of fibrin layers frequently occurs, which serves to strengthen the arterial wall locally.

The dynamic effects of aortic aneurysms have been studied experimentally and the results applied to clinical cases by Marey and François-Franck. These investigators concluded that the introduction of an elastic diverticulum into a periodic circulation scheme causes a damping of the pulse wave in the nearest arteries and, hence, makes the pulse smaller in these vessels. Thus, they believed that if an elastic and expansile aneurysm were situated in the innominate artery or in the aortic arch near the origin of the innominate, the right radial pulse would be smaller and the systolic pressure lower. If, on the other hand, the aneurysm involved the aorta near the origin of the left subclavian, or affected this vessel itself, the pulse and blood-pressure in the left arm would be smaller. The *pulsus differens,* as the difference in the two radial pulses has been termed, has, therefore, attained a certain diagnostic significance. Associated with the smaller pulse beat is a slower rise. This is due to the fact that the arterial system which, from a dynamic point of view, represents a poor system for transmitting the details of the central pressure variations to the periphery, becomes even less efficient when its volume-elasticity coefficient $\left(\frac{d\ p}{d\ v}\right)$ is further decreased by the introduction of an elastic sac. It is difficult to understand, however, why an aneurysm below the origin of the innominate should not affect the height of the pulse in the entire arterial system, rather than, as François-Franck maintained, the pulse in the right radial artery alone. If it be recalled that the velocity of the pulse wave is directly proportional to the elasticity coefficient and the thickness of the arterial wall, it can readily be seen that the rise of the pulse wave will be delayed in the vessels beyond the aneurysm. Thus, if the aneurysm be situated on the ascending aorta, the delay will be equal in both radials; if it affects the innominate, the right radial will be delayed; while if it affects the subclavian or its origin, the left radial will be delayed. This delay is of greater diagnostic value than any change in size and contour.

The expansile pulsation of the aneurysm itself occurs in two stages, as published graphic records show. The rise of such tracings is at first very steep, then becomes more gradual (Draper). There is no doubt that optical tracings would reveal even more important details, but such records, to the writer's knowledge, have not yet been reported.

The effect that an aneurysmal sac has upon the volume flow of blood and the velocity in the vessels peripheral to the aneurysm

is of even greater importance. Since the output of the heart is unaltered, the total peripheral flow is unchanged. Artificial circulation experiments indicate that if the aneurysm is situated in the ascending arch of the aorta the flow in the branches corresponding to the two radials is equal, but the stream is more constant. The pulse tends to be anacrotic. During systole more blood is accommodated in the more capacious arterial system and during diastole the flow is greater. If the aneurysm affects the innominate, the volume flow through the branches corresponding to the right radial is reduced and the flow is less intermittent than in the left. The reverse occurs when the aneurysm is at the origin of the left subclavian.

Clinical Manifestations.—The clinical manifestations of aortic aneurysm are due almost entirely to pressure and so depend largely upon their location; hence, it is desirable to consider separately the symptoms and signs of aneurysms involving: (*a*) The ascending aorta; (*b*) the innominate or its origin; (*c*) the aortic arch; (*d*) the descending aorta.

(*a*) *Aneurysm of the Ascending Aorta.*—If the aneurysm occurs within the pericardial sac, it manifests itself by many symptoms. Attacks of breathlessness and cardiac asthma associated with precordial pains of anginoid character usually occur. They are largely traceable to the fact that the pericardial space is encroached upon and the heart action mechanically interfered with. If the aneurysm is large, the entrance of venous blood is impeded. Hence, signs of venous engorgement and edema occur in the neck, arms and hands, which may become considerably swollen. Evidence of a diminished ventricular output is shown by the smaller pulse and pulse pressure in both arms. A pulsation may be visible in the second or third interspace. The roentgen-ray plates may show a normal shadow, but, when taken in the left posterior to the right anterior direction, a ratchet-shaped enlargement appears.

Aneurysm of the ascending aorta occurring external to the pericardium manifests itself in an entirely different way. The symptoms are less pronounced and occur only when the tumor becomes very large. The compression of the superior vena cava causes a venous engorgement of the face and neck, particularly on the right side. Dyspnea from encroachment upon the intrathoracic space, and pain, due to erosion, are then present.

The physical signs are very definite. The enlargement occurs to the right and forward and, by displacing the vena cava and lung, makes its appearance in the second and third interspaces to the right of the sternum. In the earlier stages, when the aneurysm comes in contact with the chest wall only, palpation over this region reveals a shock synchronous with the first sound and, more rarely, a diastolic shock synchronous with the second sound. Upon auscultation, a systolic murmur is heard in addition to the heart sounds. If the

aneurysm is adherent to the trachea, the well-known systolic tracheal tug described by Oliver can be elicited. When enlargement continues so that a forward pressure occurs, and especially when erosion of bone and cartilage has begun, the pulsation becomes visible. On palpation, its forcible and expansile character are plainly perceived. The delay in the radial pulses is uniform, but the right radial is often of smaller size. Roentgen-ray plates show an enlargement to the right of the sternum in the second to the fourth interspaces.

(b) *Aneurysm of the Innominate Artery or its Origin.*—The signs and symptoms resemble closely those associated with aneurysm of the ascending aorta, with the exception that the pulsating tumor makes its appearance high, *i. e.*, under the right clavicle. Extension backward may cause a compression of the recurrent laryngeal nerve and give rise to cough and paralysis of the right vocal cord, which gives the cough a peculiar brassy quality. Pressure upon the sympathetic may, perhaps, cause the dilatation of the right pupil often present, though it is not certain that the accompanying effects of syphilis are not accountable for this change (Babinski). The right radial pulse is smaller, more gradual in its rise and delayed more than the left. The systolic blood-pressure may be from 10 to 30 mm. lower in the right arm.

(c) *Aneurysm of the Transverse Aortic Arch.*—Inasmuch as little space is available without encroaching upon vital structures in the region where the aortic arch curves backward, aneurysms in this portion are attended by severe symptoms even when not very large. Broadbent has designated this type "the aneurysm of symptoms" as contrasted with "the aneurysm of physical signs," which applies to those arising from the ascending aorta.

The symptoms are due largely to pressure upon the surrounding structures. Pressure upon the trachea, bronchi and veins causes dyspnea, especially when the patient is reclining and the tumor mass gravitates backward. Pressure upon the esophagus causes dysphagia; upon the recurrent laryngeal, paralysis of the vocal cords with a change in voice and cough of a peculiar, brassy character. Pressure on the nerves backward produces agonizing, localized pain, while sympathetic involvement causes the pupils to become unequal, the left being usually dilated. Compression of the veins on *the left* causes the veins of the *left arm* to become dilated and swollen. As the tumor makes its way forward, it appears medially in the suprasternal notch or lifting and eroding the manubrium (Figs. 202 and 203). The characteristic heaving, expansile impulse, the sudden shock and thrill characteristic of aneurysm can be felt a short interval after the first sound. The Roentgen-ray shadow is very definite. The long, narrow shadow normally cast by the intrathoracic vessels is replaced by a broad shadow superimposed upon that of the heart (Fig. 203). The pulses differ on the two sides, being delayed and smaller on the left.

Stewart, who measured the blood flow in such cases, found it almost equal in the two hands, a fact which indicates that, although an

FIG. 202.—Photograph from case of aneurysm of arch of aorta. (After Adami and McCrae.)

FIG. 203.—Roentgenogram from case of aneurysm of aortic arch. (After Grödel.)

aneurysm distorts the shape of a pulse curve, it does not diminish the volume flow.

(*d*) *Aneurysm of the Descending Aorta.*—The aneurysms of the descending aorta cause their symptoms chiefly by pressure on nerves emerging from the spinal cord. Thus may be explained the lancinating pains either in the shoulders, sides or abdomen, depending upon the region affected and the areas of hyperesthesia. The pulsation may be visible posteriorly to the left of the spinal column or the shock and sounds may be heard only in this region.

ARTERIOSCLEROSIS.

Functionally, arteriosclerosis may be considered as a condition in which the elasticity and distensibility of the arterial wall are reduced or abolished by proliferative and degenerative changes in the intima, media and adventitia. The question as to whether the intimal proliferation is a primary inflammatory one or a compensatory thickening (Virchow, Thoma); whether it is entirely secondary to changes in the media and adventitia (Koster, Marchand, etc.); or whether these occur independently though simultaneously (Ophüls), belongs to the field of pathology and need not concern us here.[1]

Pathological Physiology.—As far as the effects of arteriosclerosis on the circulation are concerned, we may divide them into two classes, viz.: Those that affect the large elastic arteries (aorta, carotid, brachial, radial, femoral, etc.) and those that involve the peripheral arteries and arterioles, in the media of which muscle fibers predominate.

The more nearly the semi-elastic vessels approach the condition of inelastic tubes the more rapidly the pulse is propagated to the periphery. This occurs because physically they form a more perfect conducting system.

As a consequence of the reduced distensibility, the quantity of ejected blood cannot be accommodated in the aorta and, hence, a larger onward displacement occurs during systole. During the subsequent diastole, however, less elastic or potential energy is available to move the blood onward, hence the flow and pressure both diminish rapidly. The result is a tendency toward an intermittent flow at the periphery and a rapid drop of the pulse wave in diastole. It is apparent that, through this factor, the peripheral pulse, in addition to its early rise and small amplitude, changes its shape, in that the descending limb is rapid (*cf.* page 125).

When the large elastic vessels undergo sclerotic changes, their distensibility for equal pressure increments diminishes. The difference from normal vessels is schematically indicated in Fig. 204. In a normal relaxed vessel the relative increase in cubic contents, as

[1] For a recent review dealing with pathology and etiology of arteriosclerosis, consult MacCallum (Physiol. Rev., 1922, **2**, 70).

shown by the width of the lines, decreases with an increase of pressure. Hence, a pulse pressure of 20 mm. would give a greater excursion between 40 and 60 than between 100 and 120, while this, in turn, would be greater than the excursion between 180 and 200. If, however, an artery is tonically contracted, the lower pressures do not cause as great an extension as moderate ones sufficient to overcome the tonicity of the arterial wall. Thus, a pulse pressure of 20 mm. might cause a larger excursion between 100 and 120 than between 40 and 60, although at still higher pressures the amplitude would be diminished, for example, between 180 and 200 (MacWilliam, Fürst and Soetbeer, etc.). In arteriosclerotic vessels the expansion also diminishes progressively with increments of pressure provided the muscular tonus is absent. When contracted tonically, however, the expansion may

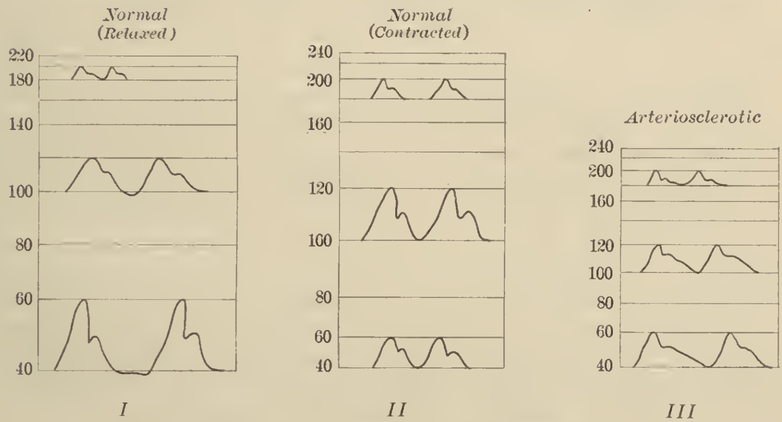

FIG. 204.—Three diagrams illustrating the effect of equal intra-arterial pressure changes on the pulse amplitude at different diastolic pressures. *I*, normal arteries, relaxed; *II*, normal arteries under tonus; *III*, arteriosclerotic arteries.

be irregular. In either case the expansion for corresponding increments of pressure will be less than in the normal arteries. Thus, in the arteriosclerotic artery, the expansion between 40 and 60, between 100 and 120 and between 180 and 200 will always be less than at corresponding pressures in the normal arteries.

We may now inquire what effect the peripheral sclerosis has upon the arterial circulation. Inasmuch as the endarteritis causes a reduction in the lumen of the peripheral arterioles, the effect resembles an increase in peripheral resistance, such as accompanies intense vasoconstriction. The effect on the arterial pressure is well known. The decreased peripheral flow from the arteries to the capillaries causes an accumulation of blood in the arterial circuit, and so elevates both systolic and diastolic pressures. The pulse pressure is decreased and the descending limb of the pressure wave becomes more nearly

horizontal. The pulse is also decreased in amplitude and corresponds to the high-tension pulses with gradual descent (*cf.* page 203).

Clinical Manifestations.—Although the sclerotic process may involve the vessels of one region or organ more severely or exclusively, the process is rarely restricted to either the central or the peripheral vessels alone, hence, the effect on the circulation, governed partly by the severity of the process, is the resultant of the areas involved. It seems to be generally agreed that the systolic pressure is not altered so long as the large splanchnic region remains unaffected, even when sclerosis is palpable in the large peripheral vessels. When these vessels are affected the systolic pressure is raised and the pulse pressure increases to 50 to 60 mm. (normal 30 to 40 mm.). The rate of transmission of the pulse is always increased and may vary from 10.1 to 23 meters per second (Friberger, Münzer).

The peripheral pulse may be large or small, depending upon the relative prominence of the factors before analyzed and also on the degree of cardiac hypertrophy usually accompanying arteriosclerosis.

The contours of both the central and peripheral pulses have been studied by the optical capsules of Frank (Friberger, Veiel). It appears that the central pulse (carotid) has a rounded or flat top and that the preliminary vibrations have disappeared. The peripheral pulse shows a steep rise and either a rounded top or a plateau, due to the fact that the form of the central pulse is transmitted better to the periphery. The rapid rise is accounted for by the rapid transmission of pressure in the rigid tubes. Secondary waves are often superimposed high upon the descending limb, perhaps because they are more rapidly reflected from the periphery (von Frey). Very frequently, however, there is no trace of dicrotism. The pulses obtained are not to be differentiated from those obtained when the tonus alone is augmented (*i. e.*, ice application, digitalis).

When the splanchnic vessels are involved or extensive sclerosis of the aorta above the diaphragm occurs, the heart hypertrophies, but whether in reaction to a greater blood-pressure alone or as a result of a simultaneous toxic influence, has been discussed elsewhere. The apex is dislocated to the left and the impulse is often heaving and forcible. The sounds are loud and clear, especially the second aortic sound, which is accentuated.

The radial arteries often reveal a palpable thickening, which is either diffusely distributed or arranged as nodular buttons or ring-like bands. This is of particular diagnostic significance, since it seems that in "alcoholics" these vessels are the first to be attacked. Other more superficial vessels, as the temporal, show a tortuous course, which, upon palpation, gives the impression of a stiff cord. Examination by the roentgen rays often establishes the existence of an arteriosclerotic vessel beyond doubt.

In addition to these general symptoms, other signs and symptoms

occur when the vessels of special organs, for example the heart, the brain, the kidneys and the limbs are affected. For their details, previous chapters and other text-books must be referred to.

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